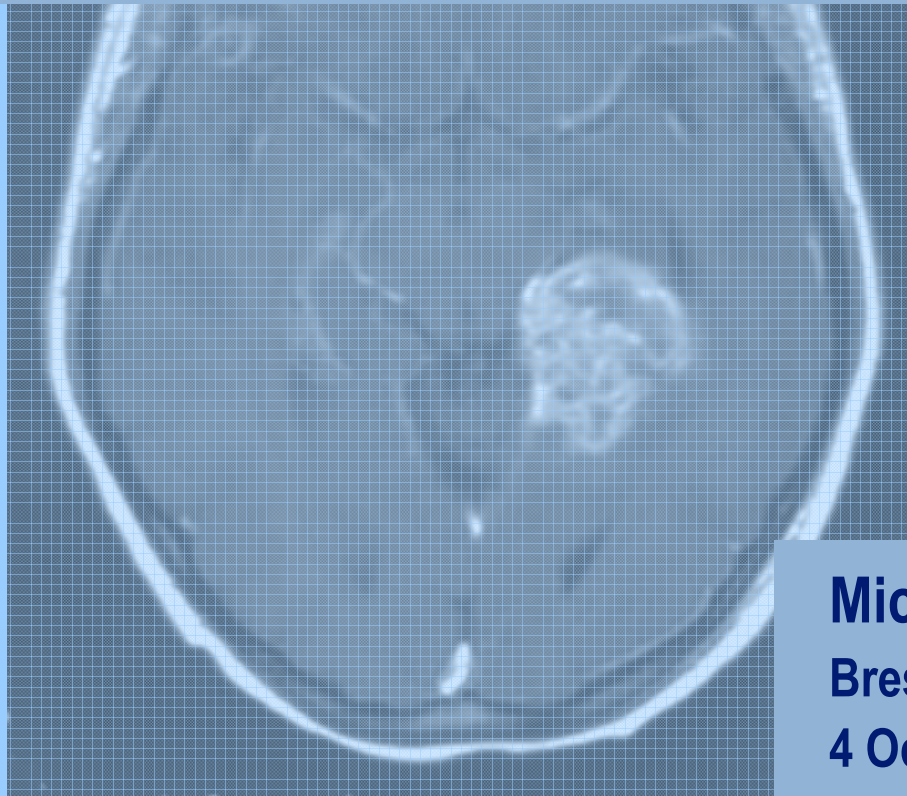


From dreams to reality

Therapy of gliomas in the elderly

for palliation, after partial surgery



Michael Brada

Brescia

4 October 2013



who is elderly

treatment options

current evidence base

Gliomas in the elderly



who is elderly

treatment options

current evidence base

Gliomas in the elderly

definition of age in the context of brain tumour

chronological age

biological age

surrogates

fitness

comorbidity

frailty index

entry into clinical trials

prognosis

Age and outcome in high grade gliomas

definition of age in the context of brain tumour

chronological age

biological age

surrogates

fitness

comorbidity

frailty index

entry into clinical trials

prognosis

Age and outcome in high grade gliomas

definition of age in the context of brain tumour

chronological age

biological age

surrogates

fitness

comorbidity

frailty index

entry into clinical trials

prognosis

trials

age limit

1980's & 1990's

65

2000's

70

Age and outcome in high grade gliomas

definition of age in the context of brain tumour

chronological age

biological age

surrogates

fitness

comorbidity

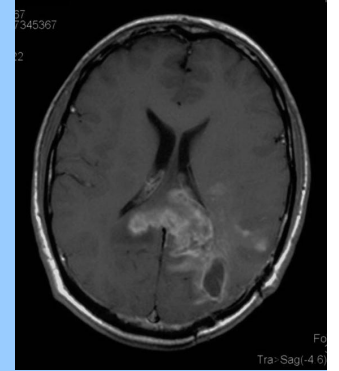
frailty index

entry into clinical trials

prognosis

Age and outcome in high grade gliomas

prognosis in GBM

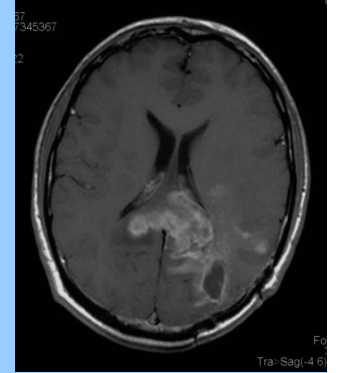


prognostic indices in <65 / 70 year olds

prognostic index in ≥ 70 years

Age and outcome in high grade gliomas

prognosis in GBM



prognostic indices in <65 / 70 year olds

prognostic index in ≥ 70 years

Age and outcome in high grade gliomas

definition of prognosis in GBM based on clinical trials
RPA index (RTOG)

age

performance status

extent of resection

neurological function (working/not working)

RPA recursive partitioning analysis

Age and outcome in high grade gliomas

Li et al Int. J. Radiation Oncology Biol. Phys., 81, (3), 623–630, 2011

definition of prognosis in GBM based on RTOG clinical trials new RPA classes

| class | age | | KPS | | KPS | | surgery | | function | |
|-------|------|-----|-----|-----|-----|-----|------------------|--------|----------------------------|-------|
| | < 50 | ≥50 | ≥90 | <90 | ≥70 | <70 | resec' | biopsy | working | other |
| III | + | | + | | | | | | | |
| IV | + | | | + | | | | | | |
| | | + | | | + | | RPA class | | median survival (m) | |
| V&VI | | + | | | + | | | | | |
| | | + | | | + | | III | 17.1 | | |
| | | + | | | | + | IV | 11.2 | | |
| | | | | | | | V & VI | 7.5 | | |

Age and outcome in high grade gliomas

definition of prognosis in HGG based on clinical trials

MRC prognostic index

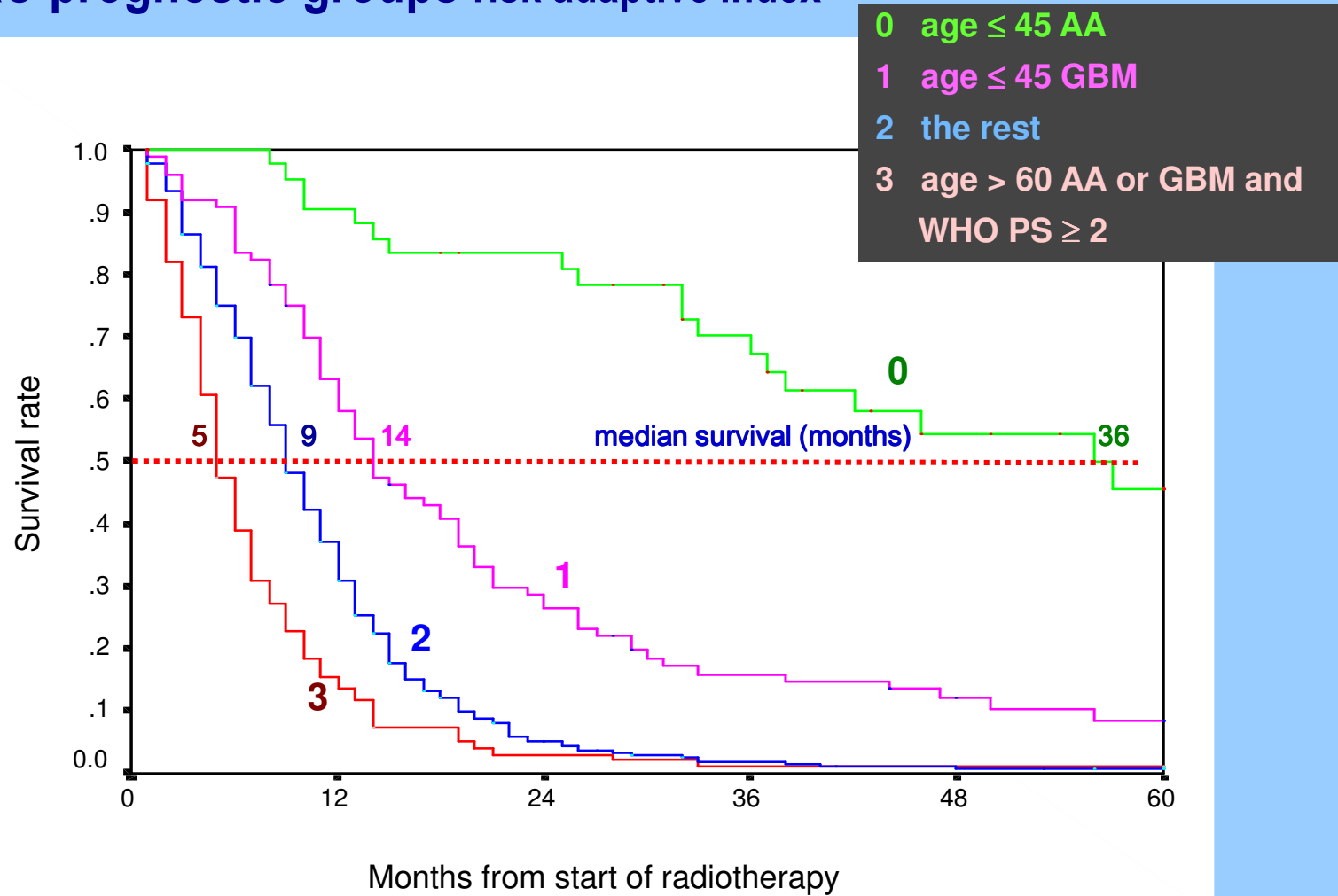
age

performance status

histology

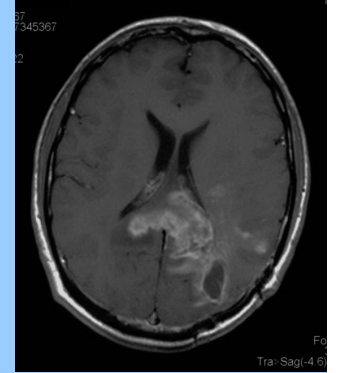
Age and outcome in high grade gliomas

MRC prognostic groups risk adaptive index



High grade glioma prognosis

prognosis in GBM



prognostic indices in <65 / 70 year olds

prognostic index in ≥ 70 years

Age and outcome in high grade gliomas

Prognosis in GBM in ≥ 70 s

RPA index

age (<75.5 / ≥ 75.5 yrs)

performance status

extent of resection

Age and outcome in high grade gliomas

Prognosis in GBM in ≥ 70 s

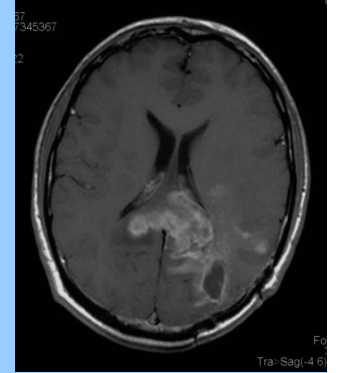
RPA classes

| | age | | KPS | | surgery | |
|-------|--------|-------------|-----------|-----|---------|--------|
| class | < 75.5 | ≥ 75.5 | ≥ 70 | <70 | resec' | hionsv |
| I | + | | | | | |
| II | | + | | | | |
| III | | | + | | | |
| IV | | | | + | | |

| RPA class | median survival (m) |
|-----------|---------------------|
| I | 9.1 |
| II | 7.0 |
| III | 4.5 |
| IV | 2.7 |

Age and outcome in high grade gliomas

Poor prognosis GBM median survival < 7.5 months



age ≥ 50

KPS < 70

KPS ≥ 70

biopsy

limited function

age ≥ 70

KPS < 70

KPS ≥ 70

biopsy

age ≥ 75.5

Age and prognosis



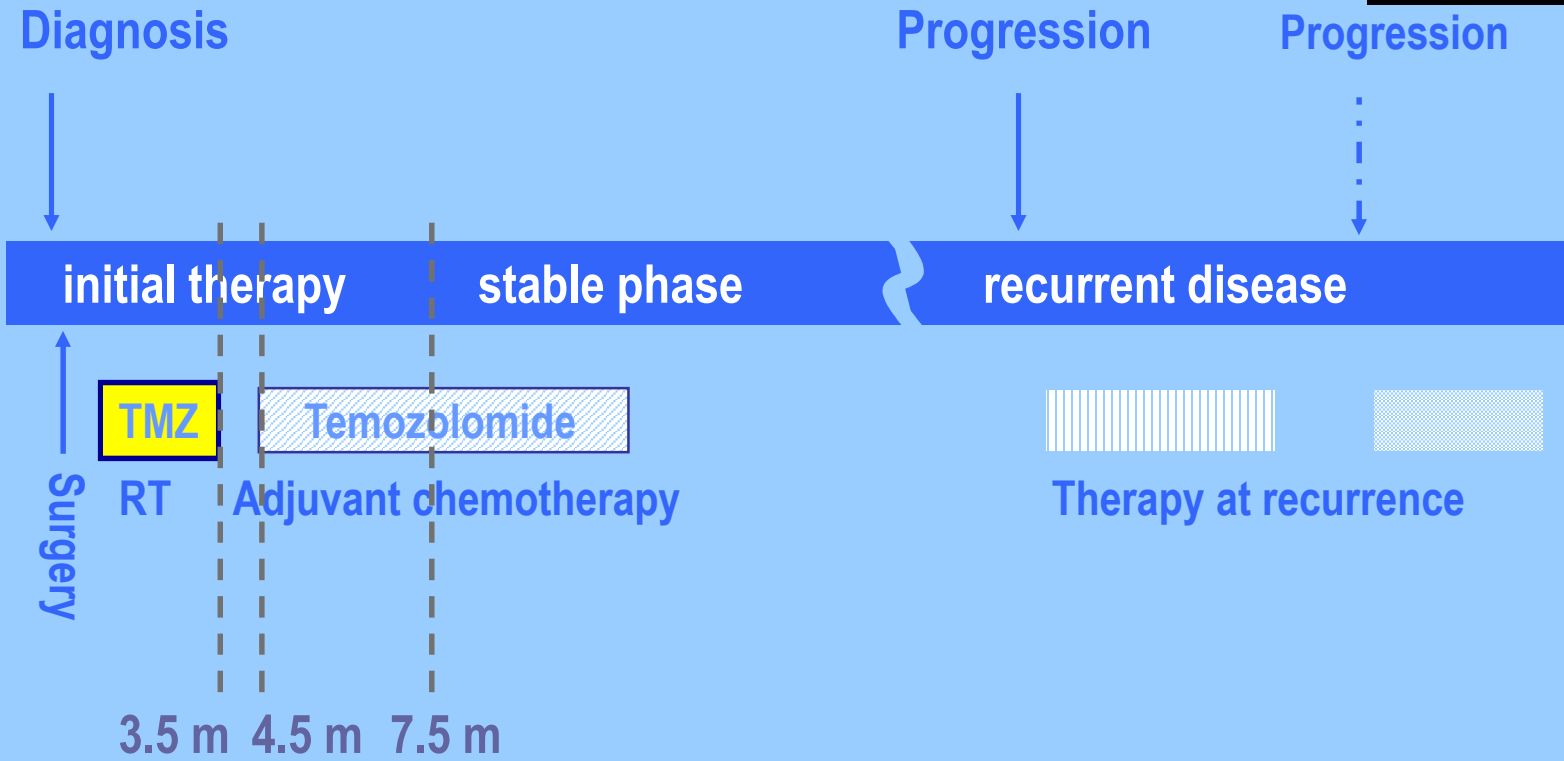
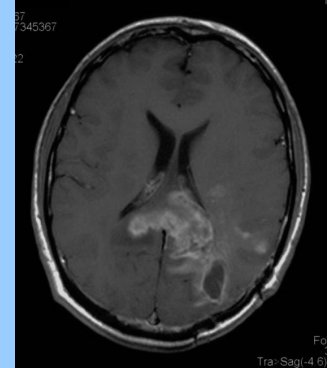
who is elderly

treatment options

current evidence base

Gliomas in the elderly

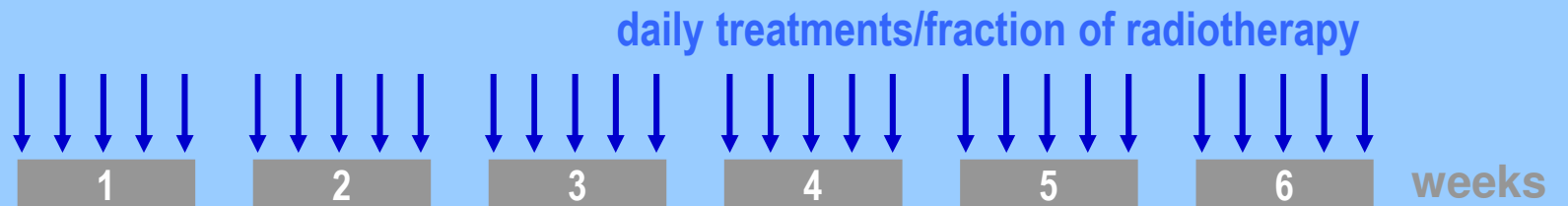
Treatment options in glioblastoma



High grade glioma therapy

Radical radiotherapy

Palliative

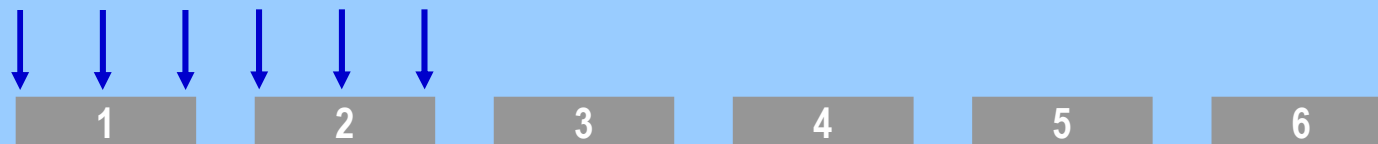


Conventional radiotherapy

60Gy 30 fractions in 6 weeks

Radiotherapy in malignant glioma

Palliative radiotherapy



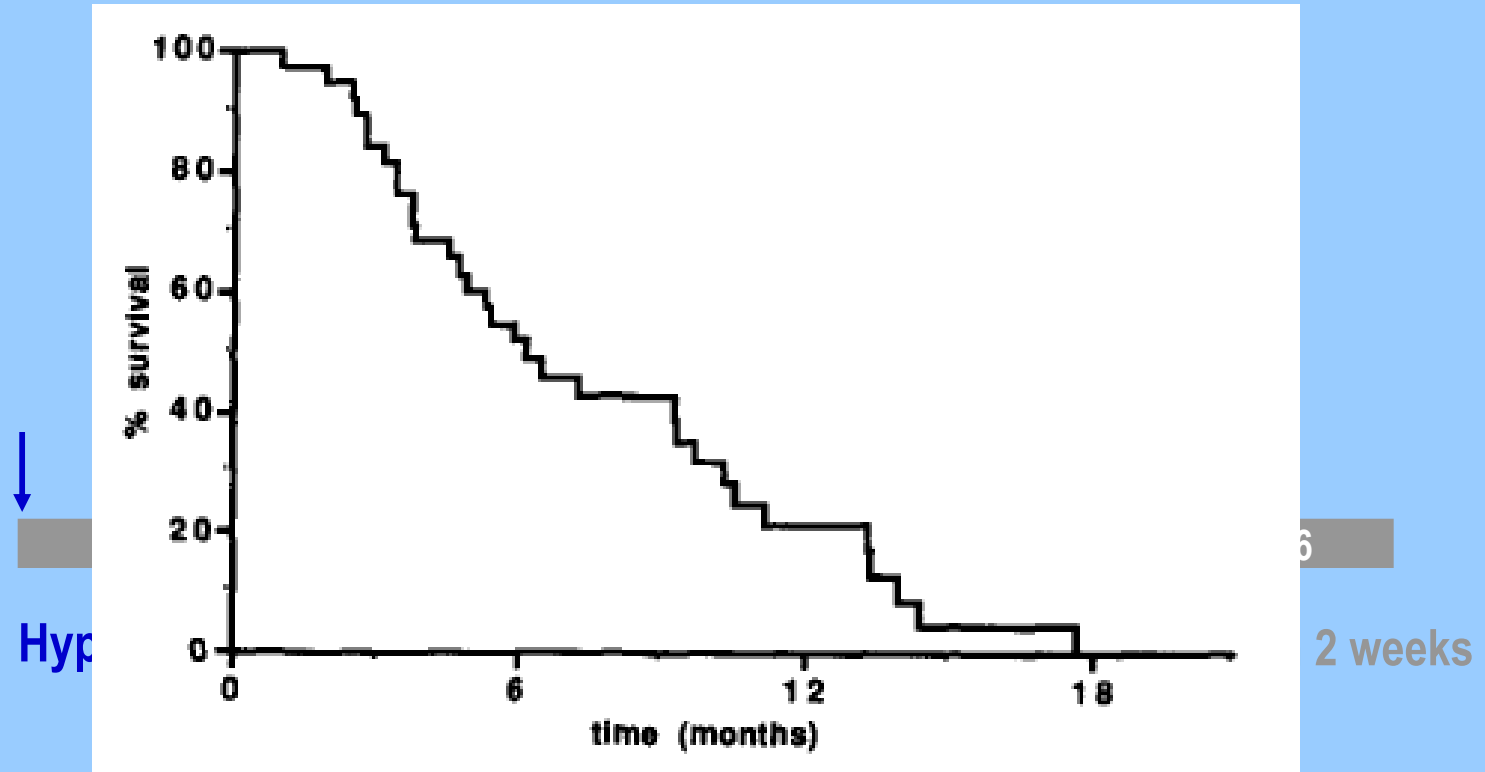
Hypofractionated radiotherapy

30Gy 6 fractions in 2 weeks

Thomas et al 1994
McAleese et al 2003

Radiotherapy in malignant glioma

Palliative radiotherapy



Thomas et al 1994
McAleese et al 2003

Radiotherapy in malignant glioma

**Single arm trial and comparison
to matched controls**

High grade glioma
poor prognosis by age and
performance status

**poor prognosis
HGG cohort (40)**

**matched cohort
from MRC BR5 study**

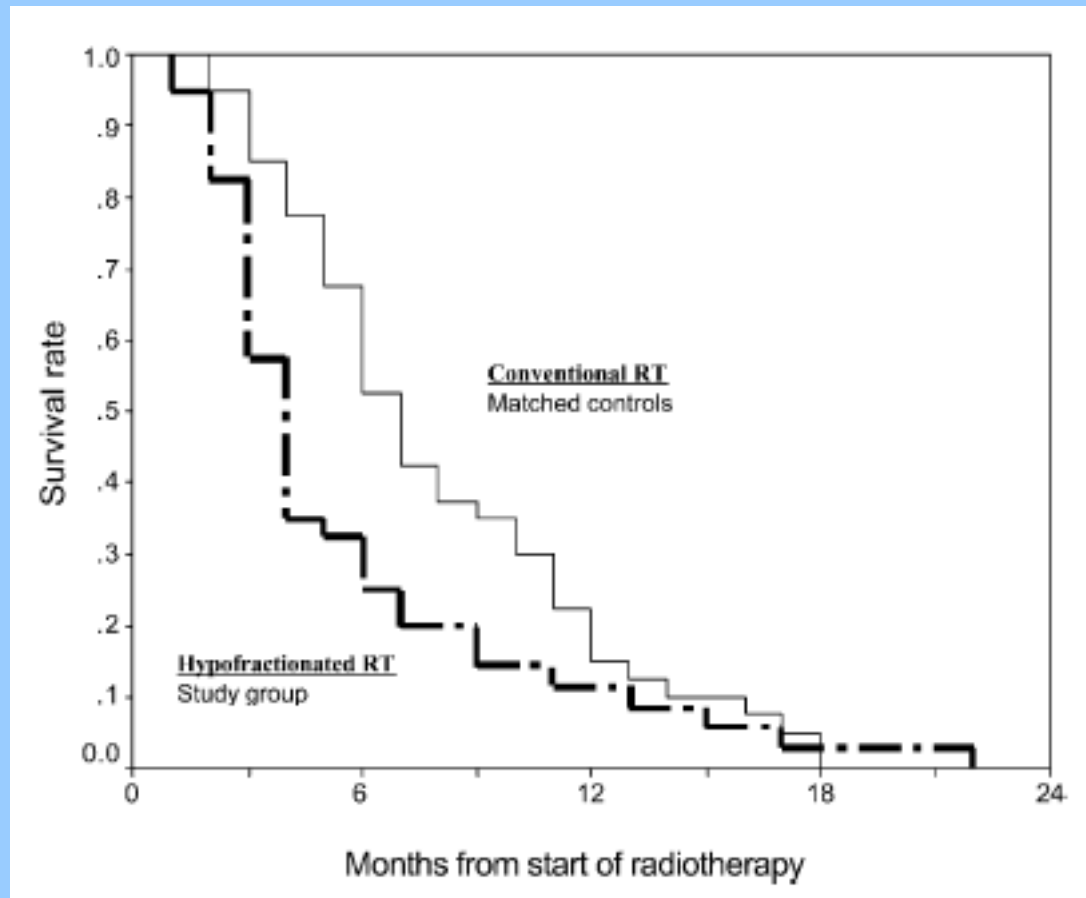


**hypofractionated
palliative RT**

**conventional
“radical” RT**

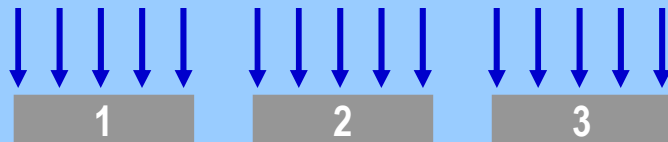
Palliative radiotherapy

Palliative radiotherapy



Palliative radiotherapy

Palliative radiotherapy



Hypofractionated radiotherapy



40Gy 15 fractions in 3 weeks

Radiotherapy in malignant glioma



who is elderly

treatment options

current evidence base

endpoints

survival

neurological
function

QOL

Gliomas in the elderly

French multicentre trial

glioblastoma
aged ≥ 70 (70-85)
KPS > 70

Histological confirmation

randomize

85 patients

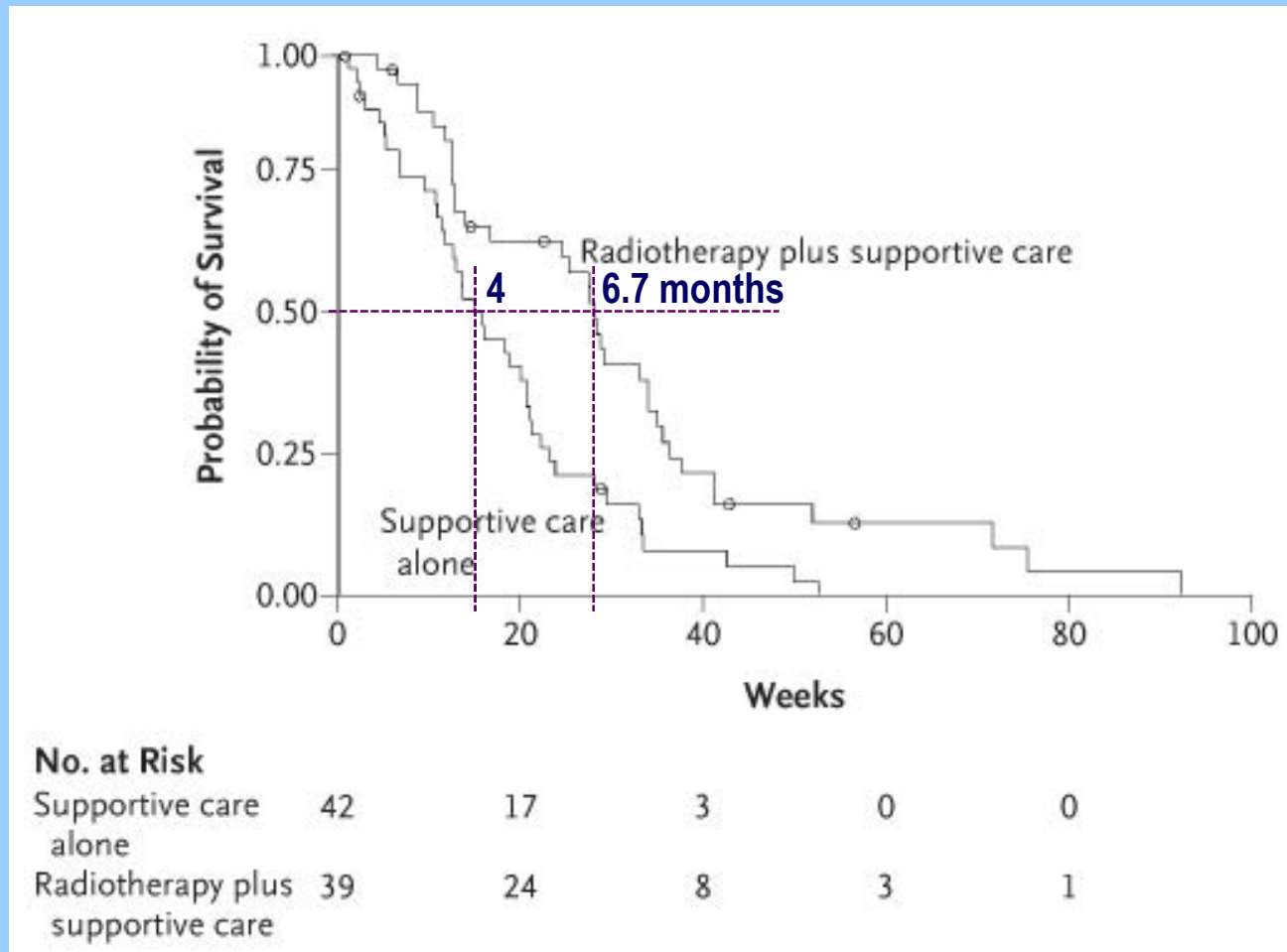
best supportive care

best supportive care +
Radiotherapy
(50Gy @ 1.8Gy/fraction)

Glioblastoma in the elderly and radiotherapy

Keime-Guibert et al 2007

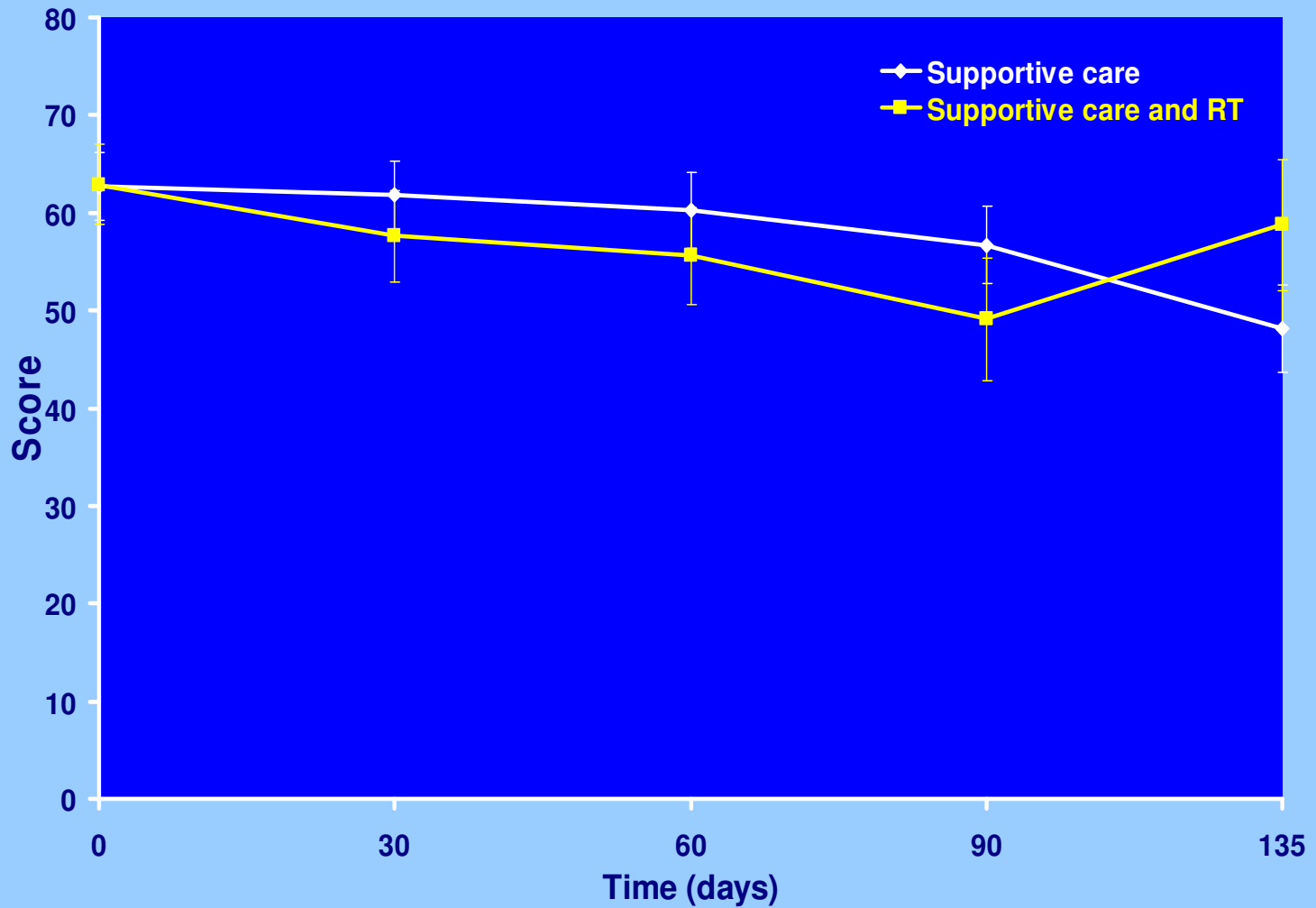
Survival



Glioblastoma in the elderly and radiotherapy

Keime-Guibert et al 2007

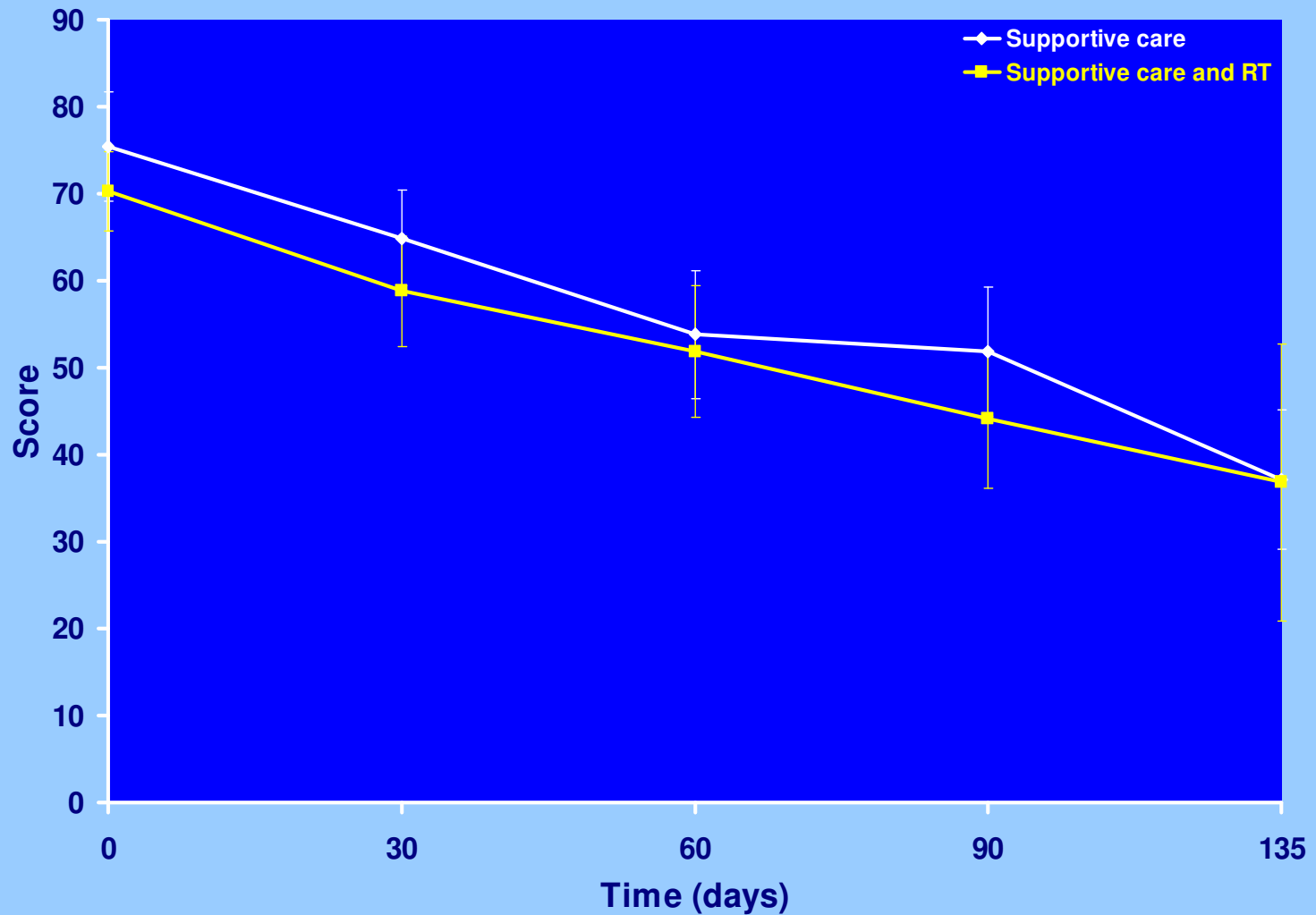
Global quality of life



Glioblastoma in the elderly and radiotherapy

Keime-Guibert et al 2007

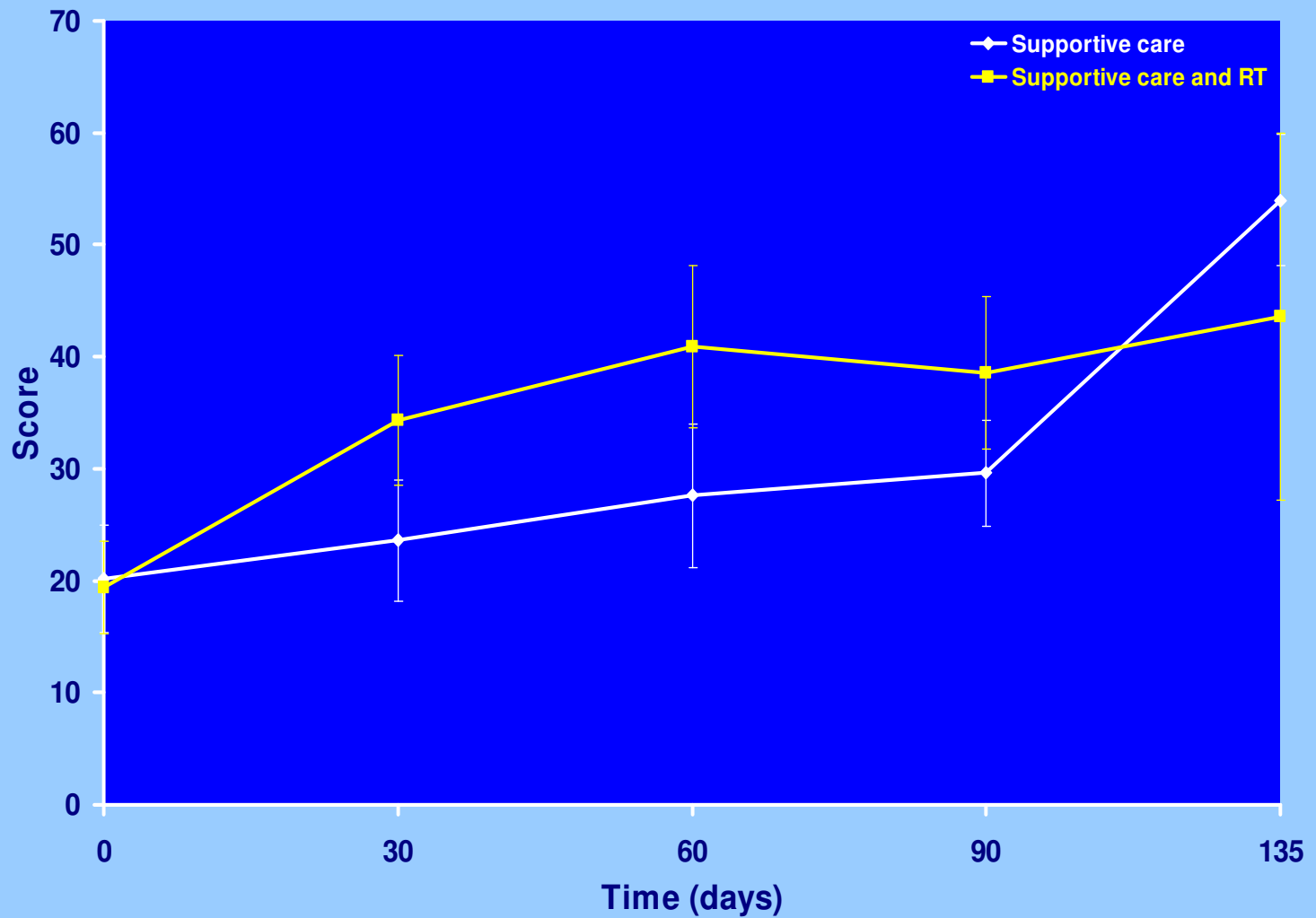
Physical quality of life



Glioblastoma in the elderly and radiotherapy

Keime-Guibert et al 2007

Quality of life - motor dysfunction

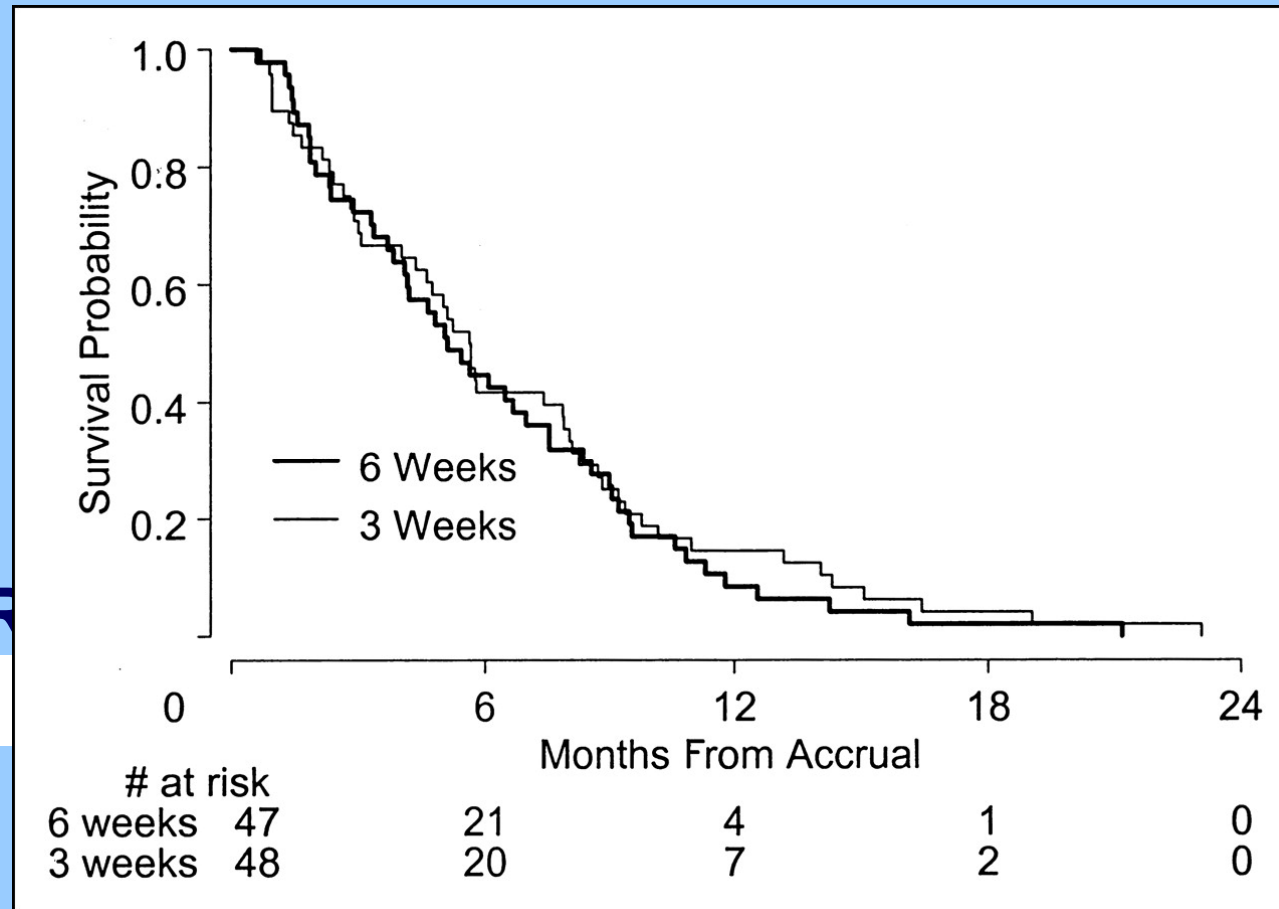


Glioblastoma in the elderly and radiotherapy

Keime-Guibert et al 2007

Canadian multicentre trial

glioblastoma
aged ≥ 60



Glioblastoma in the elderly and radiotherapy

Nordic trial

glioblastoma
aged > 60 (60-88)

Histological confirmation

randomize

Temozolomide

patients
342 enrolled
291 randomised

radiotherapy
hypofractionated

34 Gy in 10 fractions

radiotherapy
radical

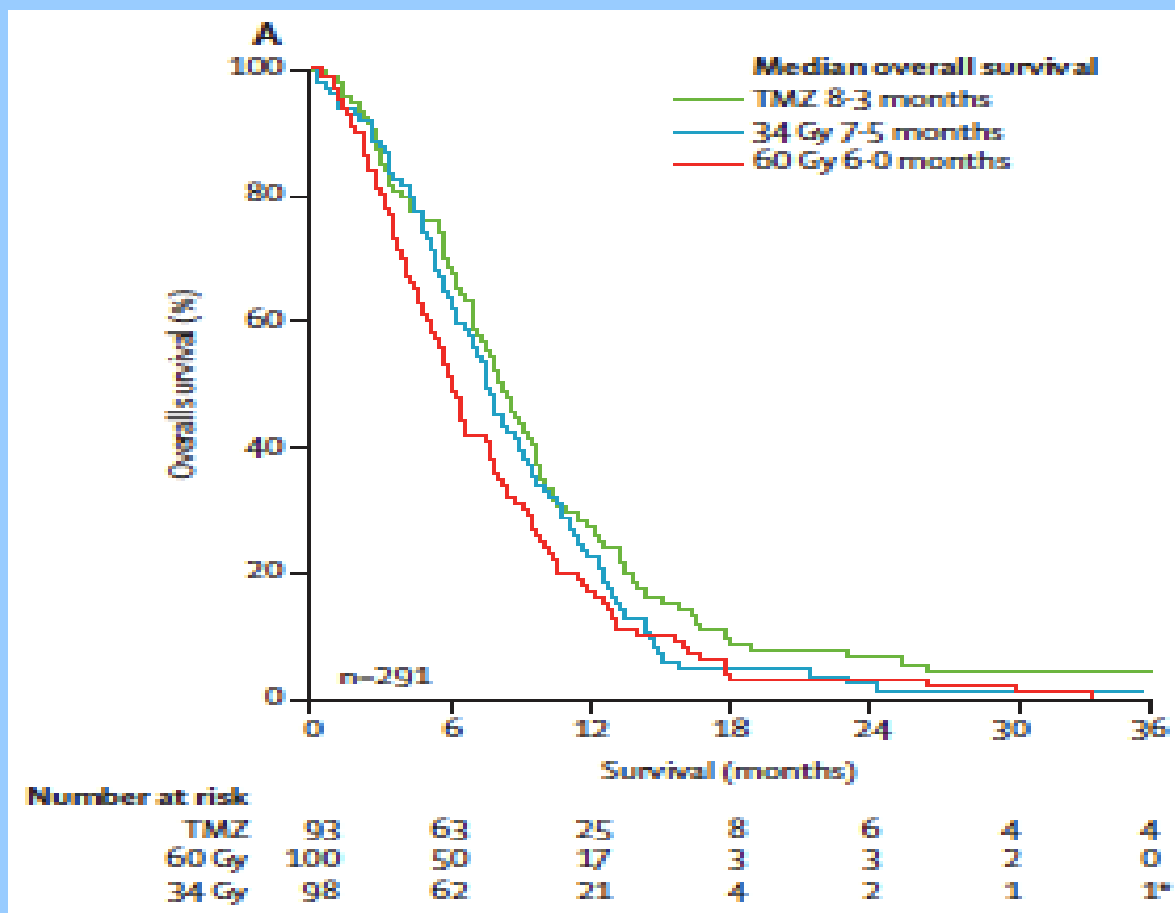
60Gy in 30 fractions

Glioblastoma in the elderly

Nordic trial

glioblastoma
aged > 60 (60-88)

survival all patients



patients
342 enrolled
291 randomised

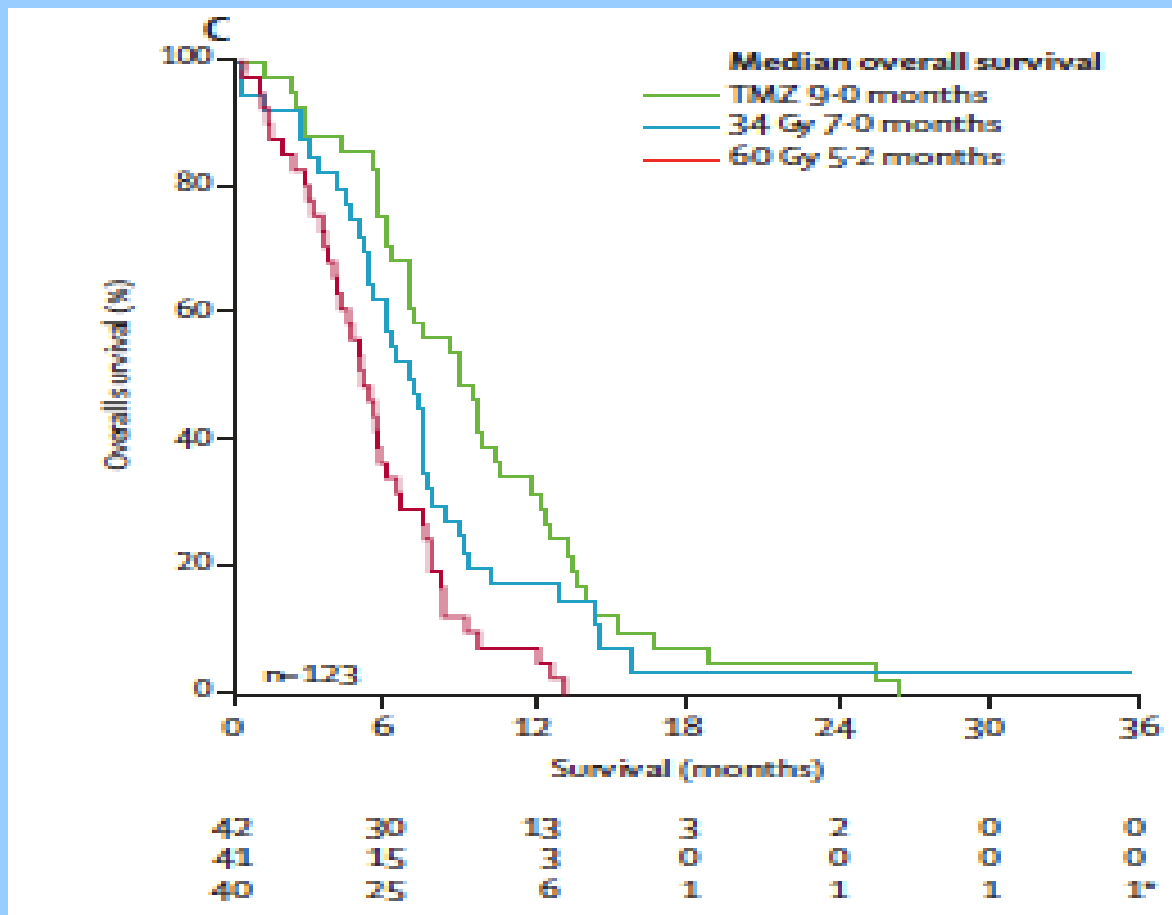
Glioblastoma in the elderly

Malmström et al 2012

Nordic trial

glioblastoma
aged > 60 (60-88)

survival in patients > 70



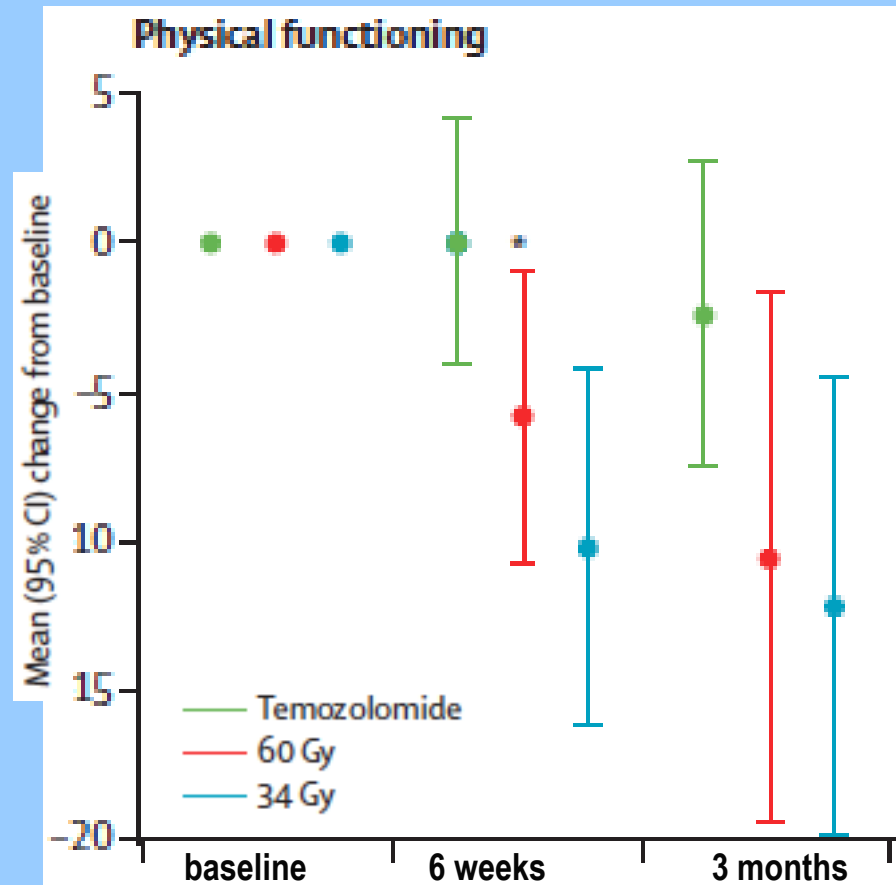
patients
342 enrolled
291 randomised

Glioblastoma in the elderly

Malmström et al 2012

Nordic trial

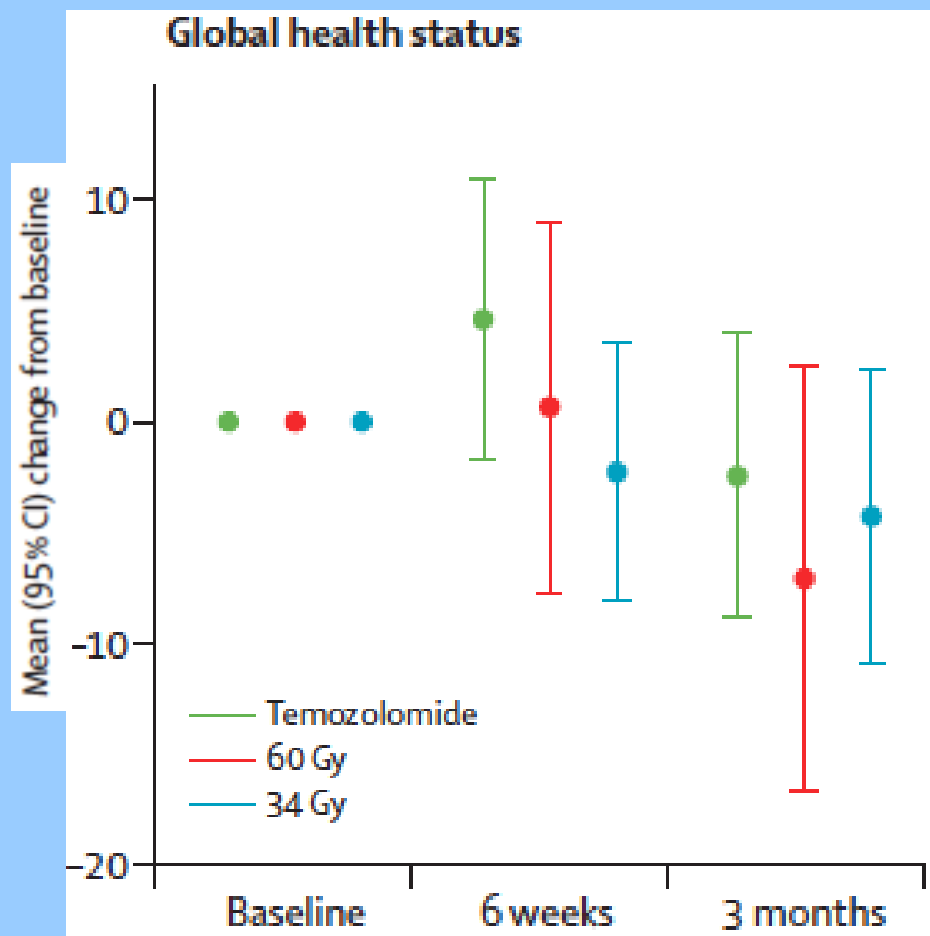
quality of life



Glioblastoma in the elderly

Nordic trial

quality of life



Glioblastoma in the elderly

German NOA-08 trial

glioblastoma &
anaplastic astrocytoma
aged > 65 (66-84)
KPS > 60

Histological confirmation

randomize

Temozolomide

radiotherapy

60Gy in 30 fractions

patients

584 screened

412 enrolled

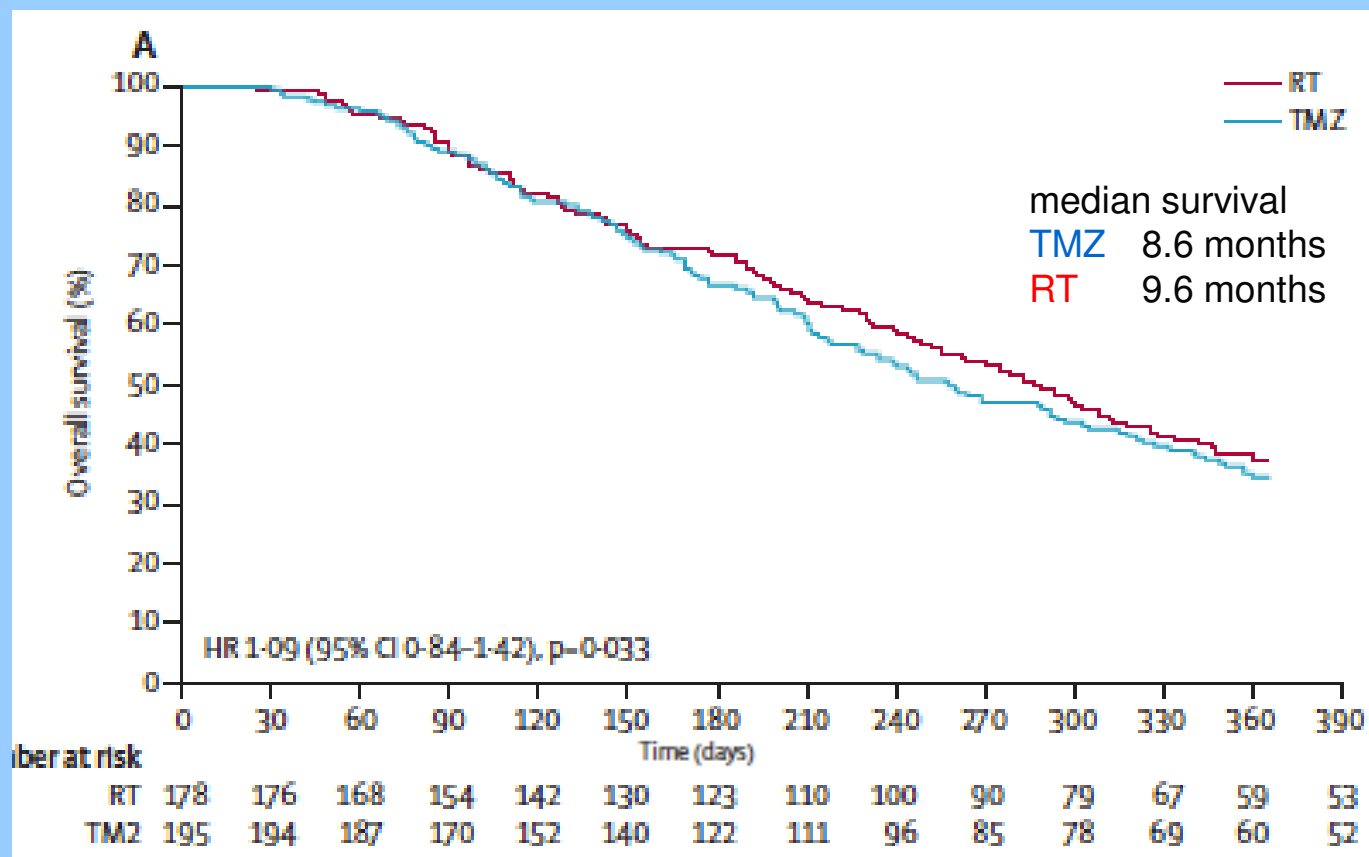
373 received at least one course of treatment

High grade glioma in the elderly

German NOA-08 trial

survival

glioblastoma &
anaplastic astrocytoma
aged > 65 (66-84), KPS > 60

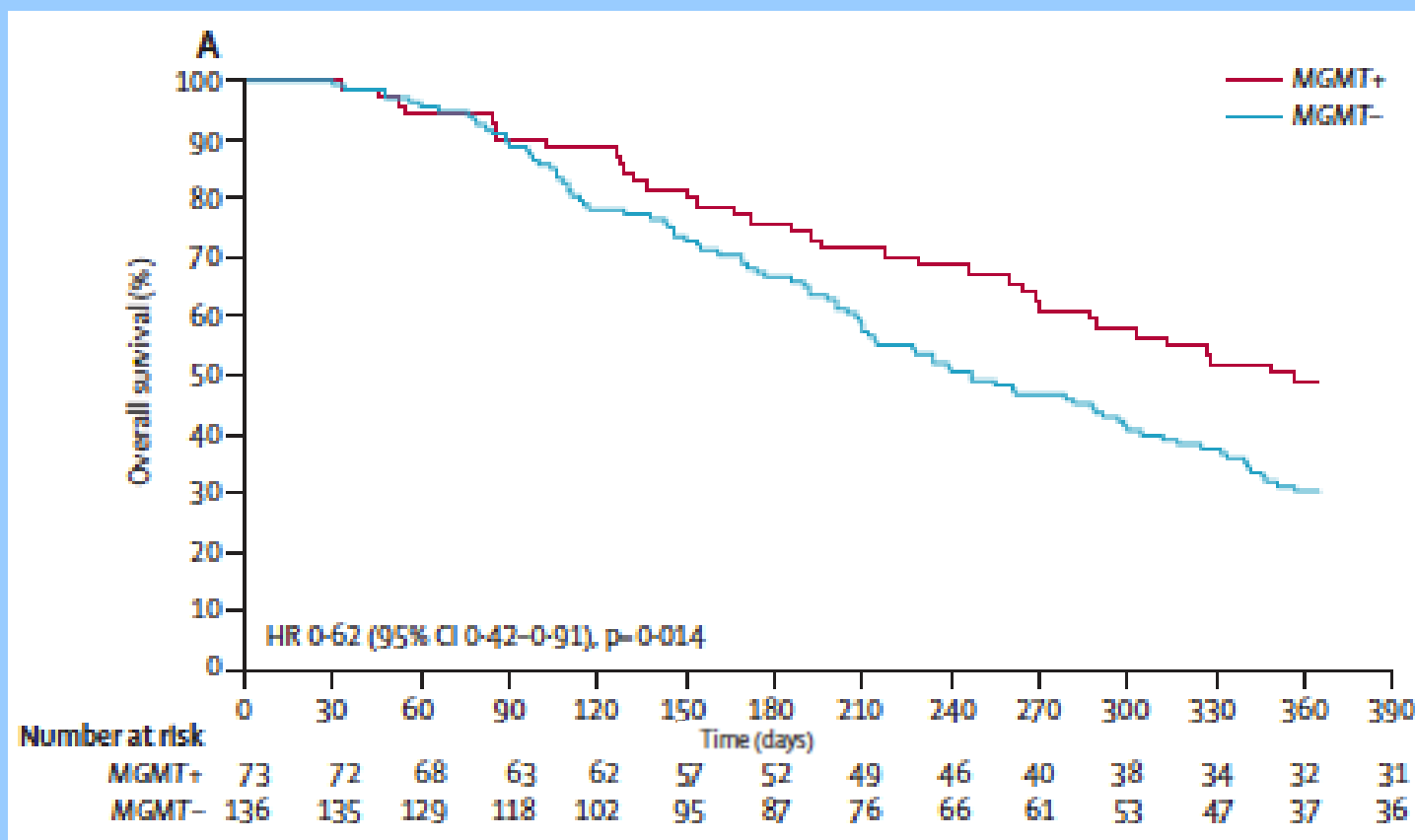


High grade glioma in the elderly

German NOA-08 trial

survival by MGMT status

glioblastoma &
anaplastic astrocytoma
aged > 65 (66-84), KPS > 60

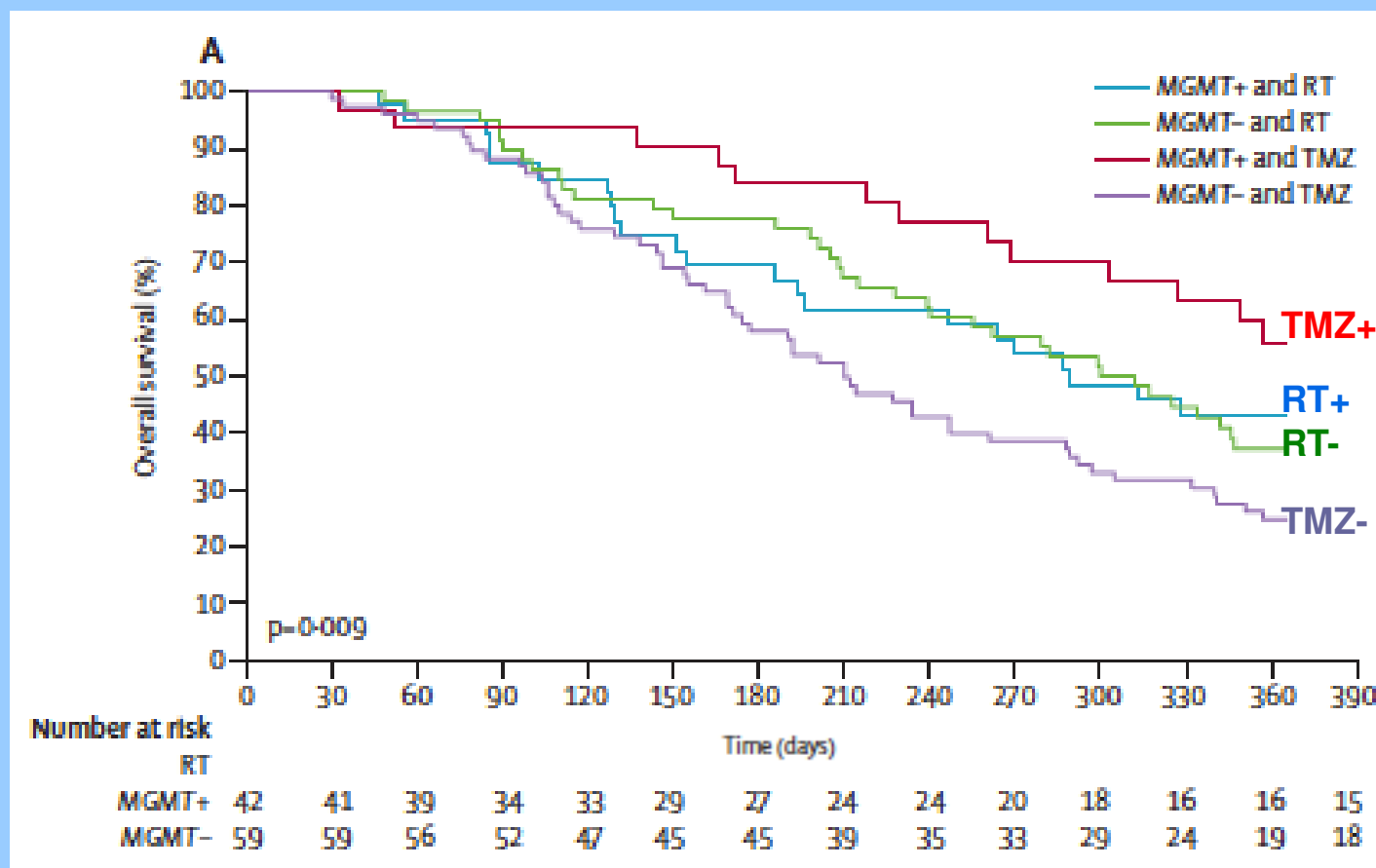


High grade glioma in the elderly

German NOA-08 trial

survival by MGMT status & treatment

glioblastoma &
anaplastic astrocytoma
aged > 65 (66-84), KPS > 60



+ methylated MGMT
- nonmethylated MGMT

High grade glioma in the elderly



who is elderly

treatment options

current evidence base

Gliomas in the elderly

Current evidence base

supportive care

radiotherapy
34 Gy in 10 fractions

radiotherapy
60Gy in 30 fractions

Temozolomide

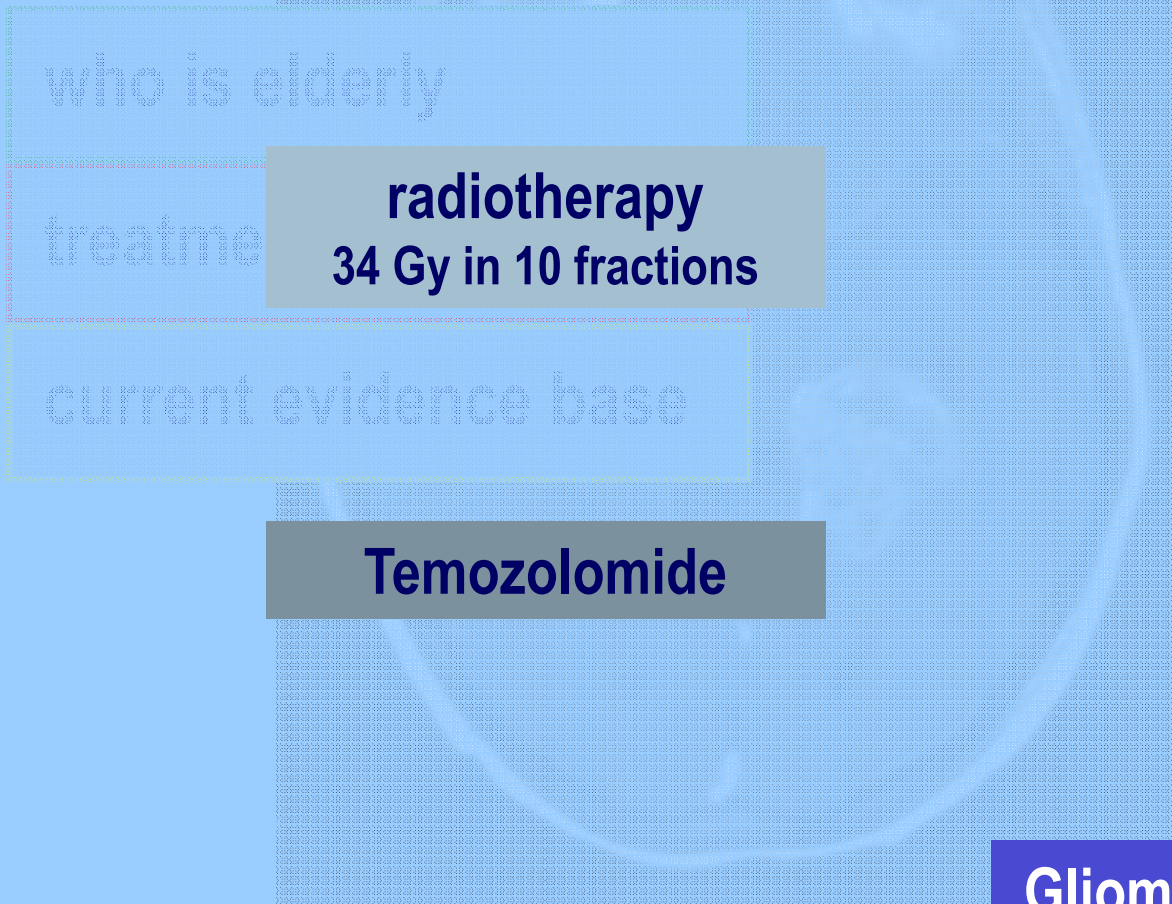
Gliomas in the elderly

Current evidence base

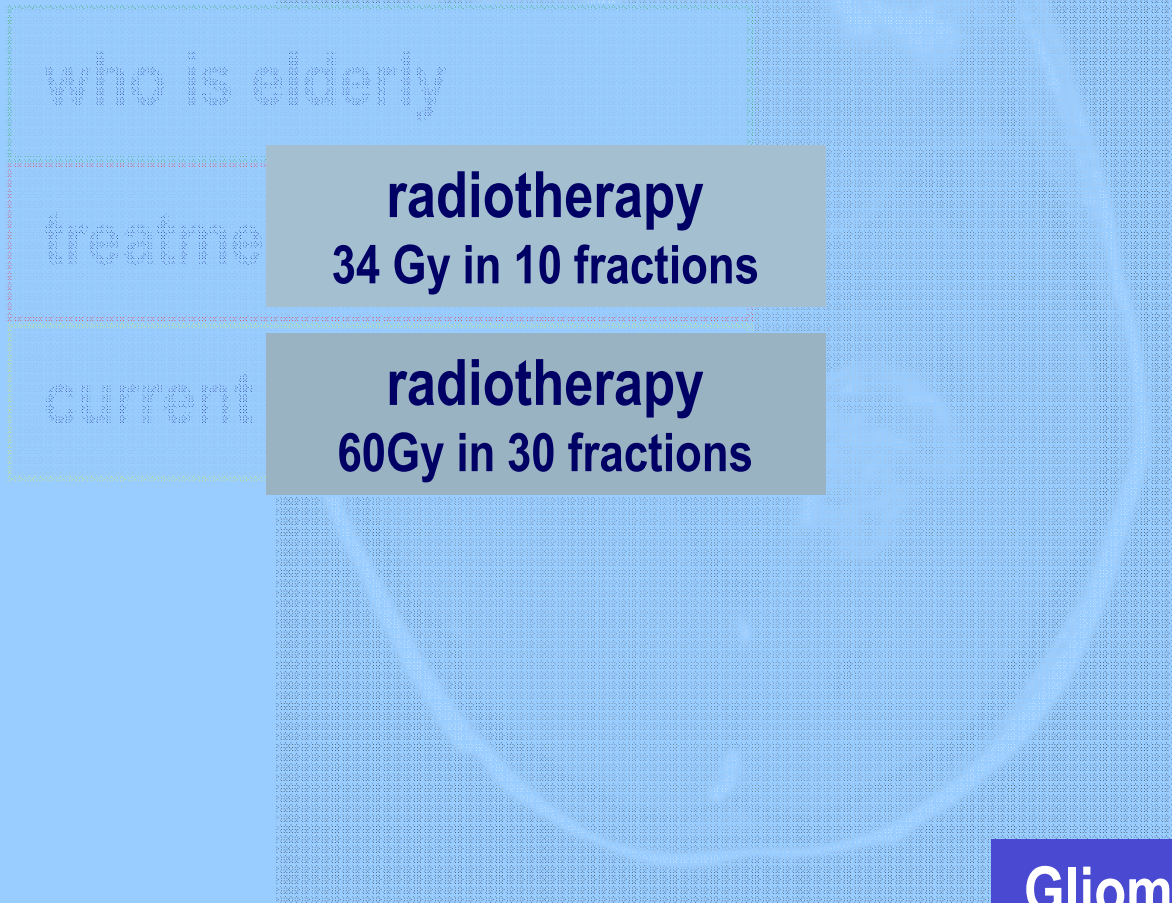


Gliomas in the elderly

Current evidence base

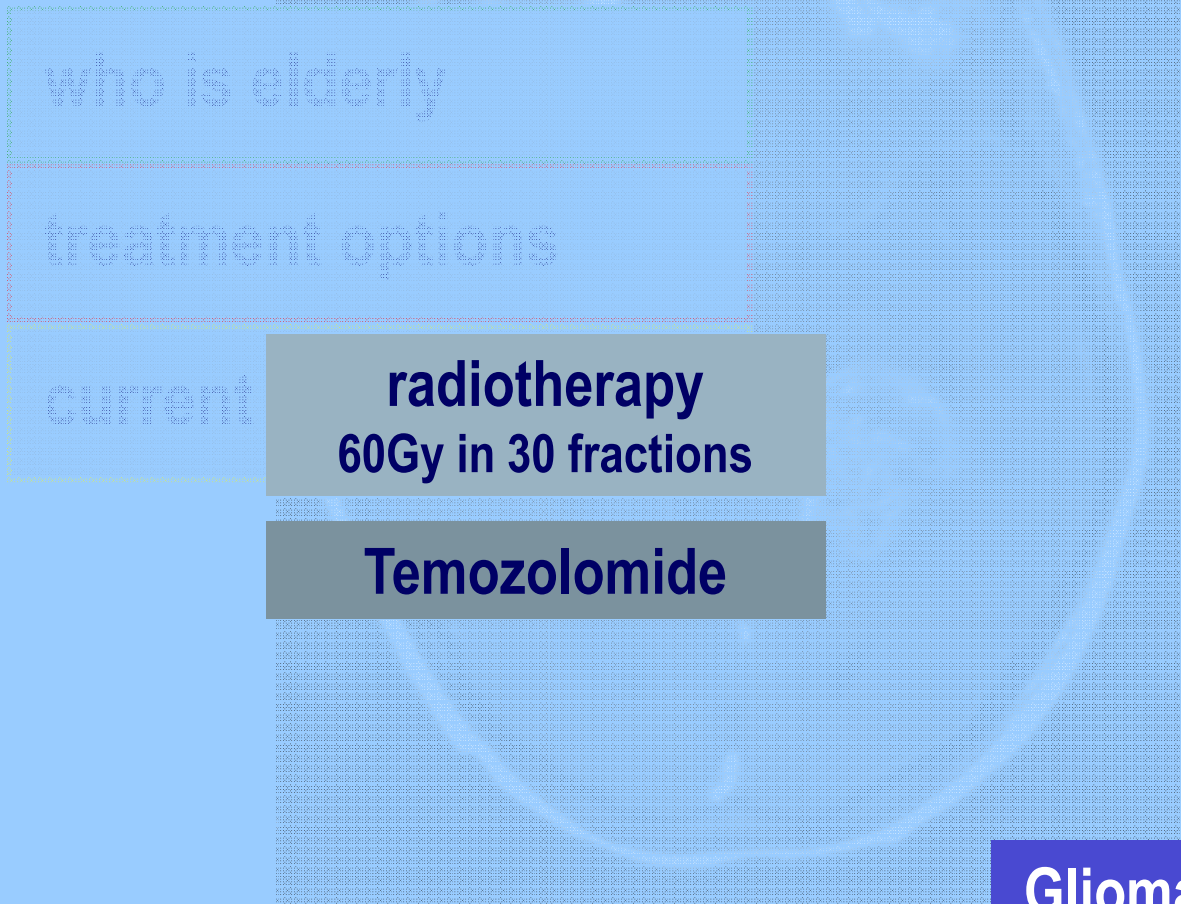


Current evidence base



Gliomas in the elderly

Current evidence base



radiotherapy
60Gy in 30 fractions

Temozolomide

Gliomas in the elderly

Current evidence base

supportive care

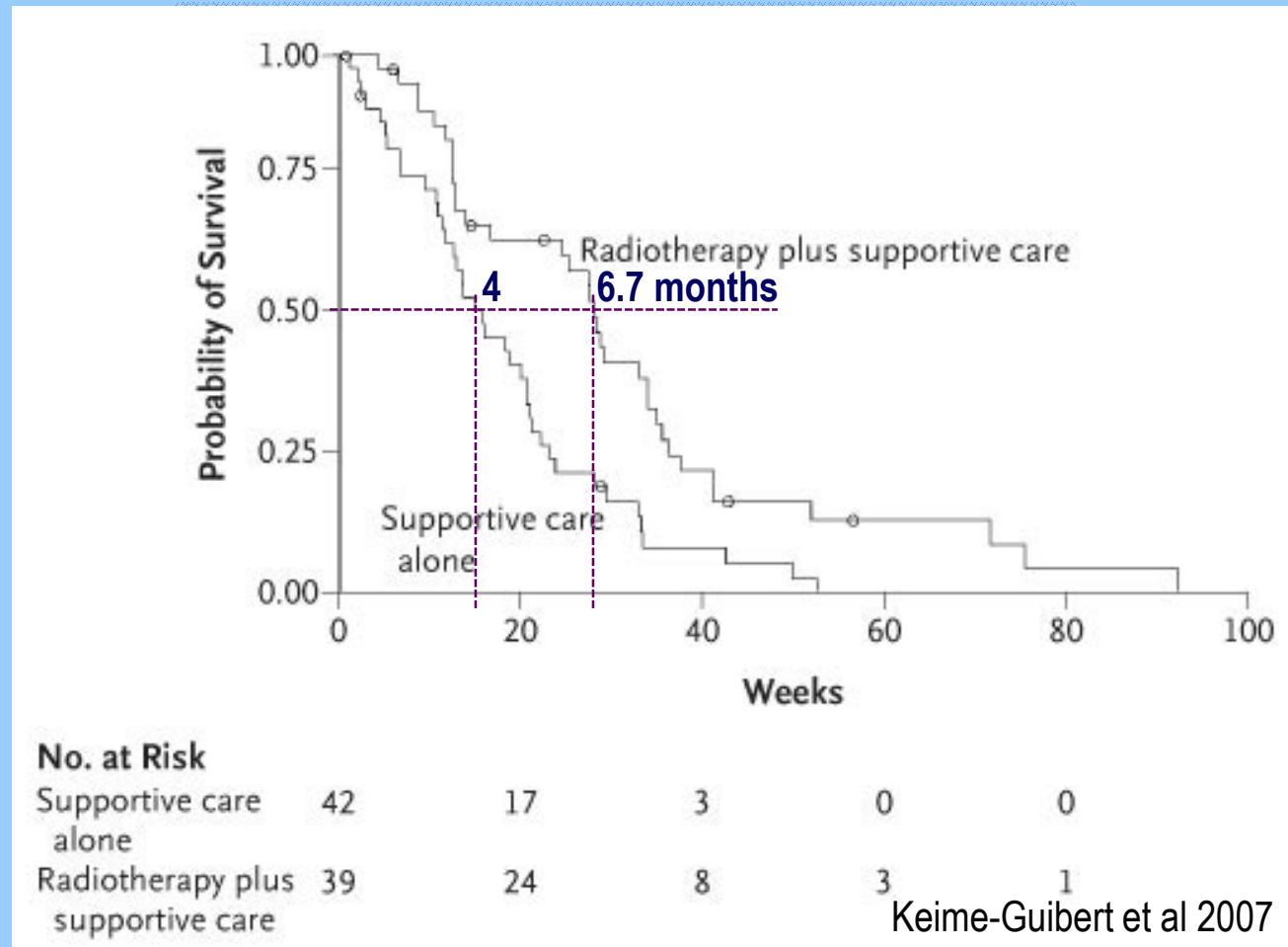
radiotherapy
34 Gy in 10 fractions

radiotherapy
60Gy in 30 fractions

Temozolomide

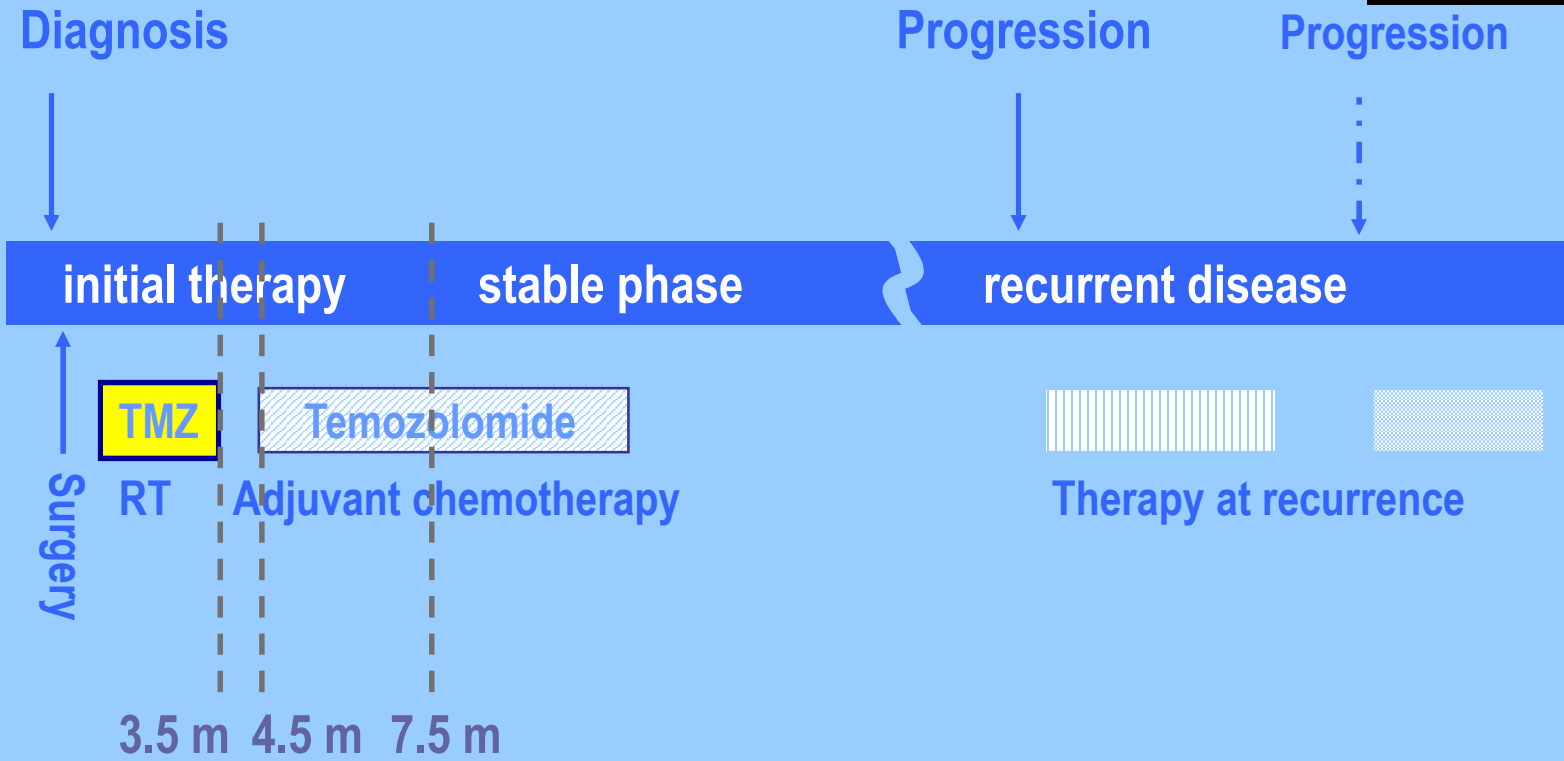
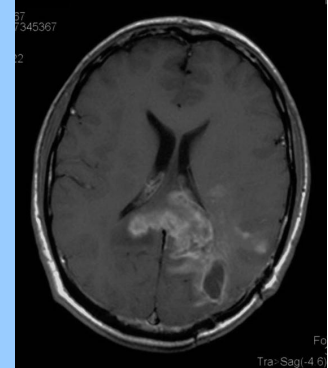
Gliomas in the elderly

Where next?



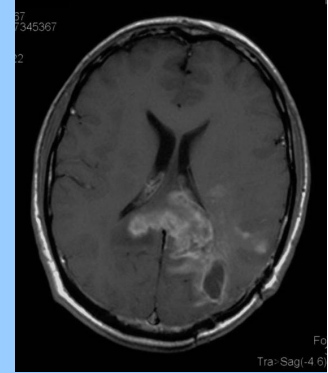
Gliomas in the elderly

Treatment options in glioblastoma

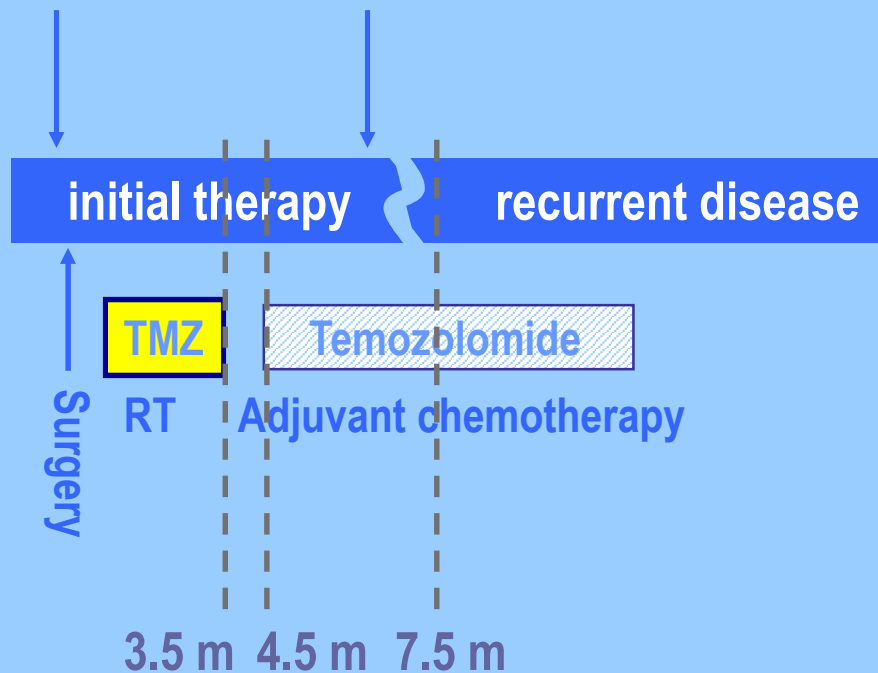


High grade glioma therapy

Treatment in glioblastoma in the elderly



Diagnosis Progression

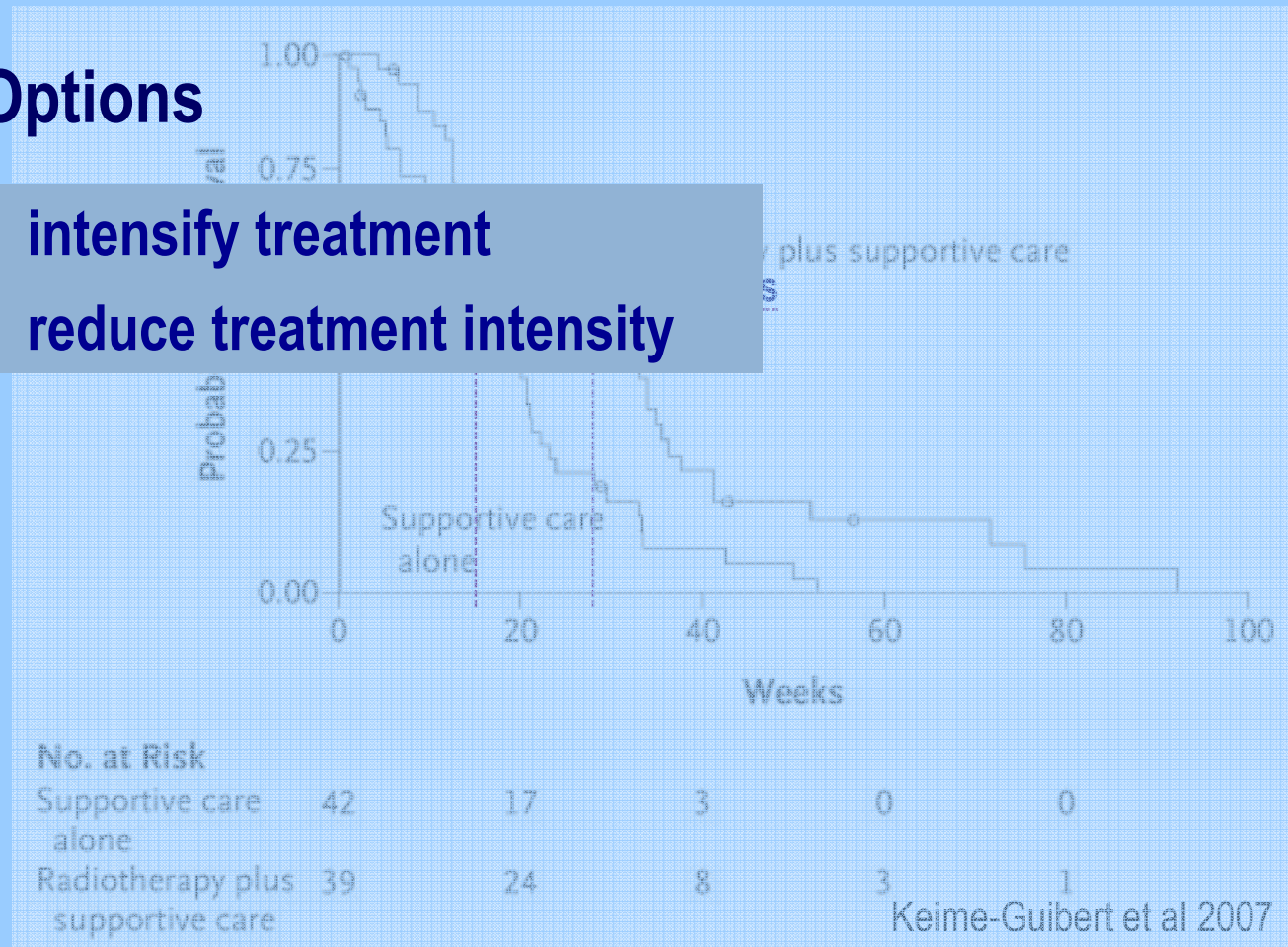


High grade glioma therapy

Where next?

Options

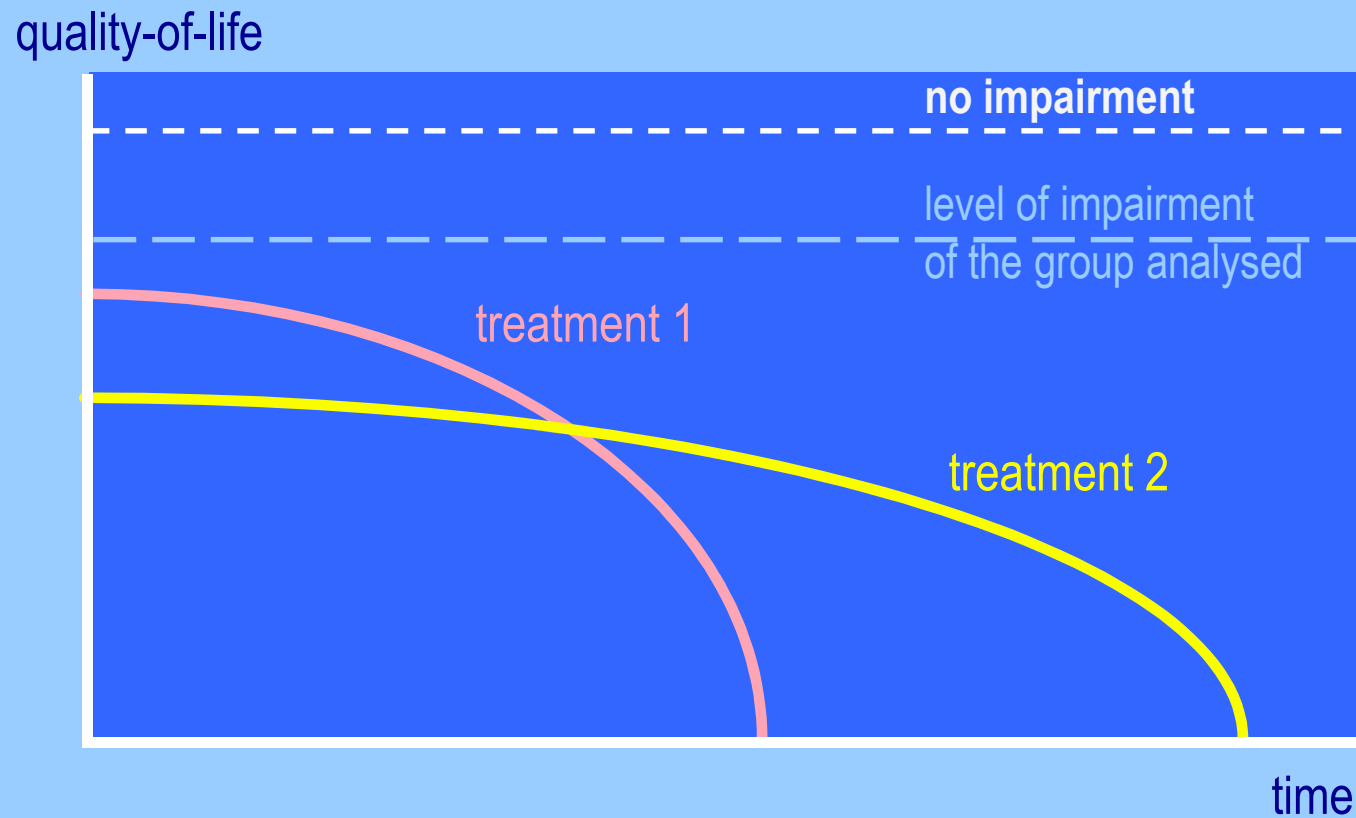
- intensify treatment
- reduce treatment intensity



Gliomas in the elderly

survival and quality of life

quality adjusted survival

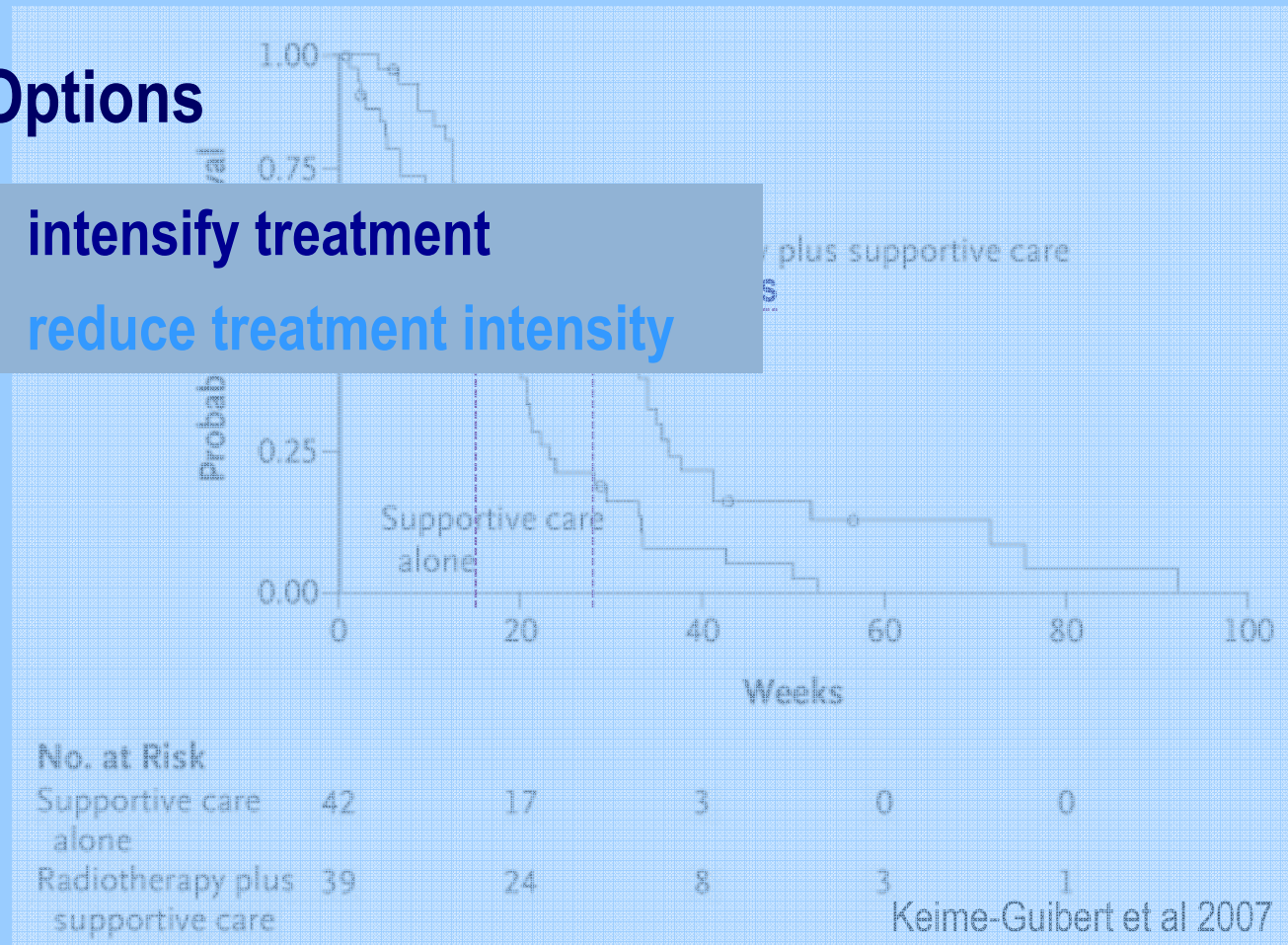


Gliomas in the elderly

Where next?

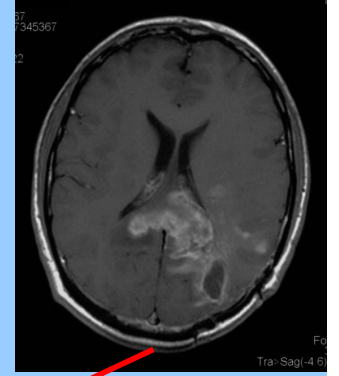
Options

- intensify treatment
- reduce treatment intensity



Gliomas in the elderly

intensifying treatment



Primary glioblastoma

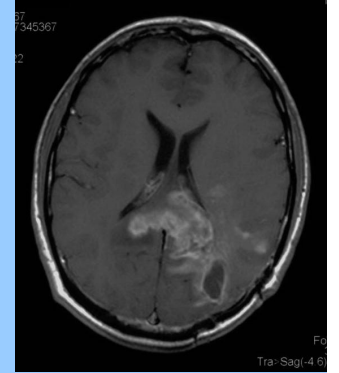
randomize

Radiotherapy
palliative

Radiotherapy
radical

Gliomas in the elderly

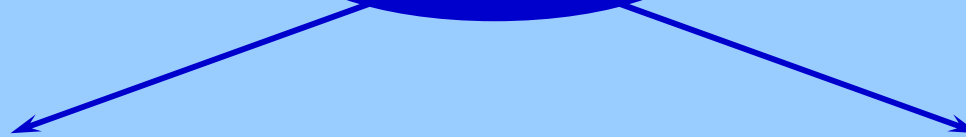
intensifying treatment



Primary glioblastoma



randomize



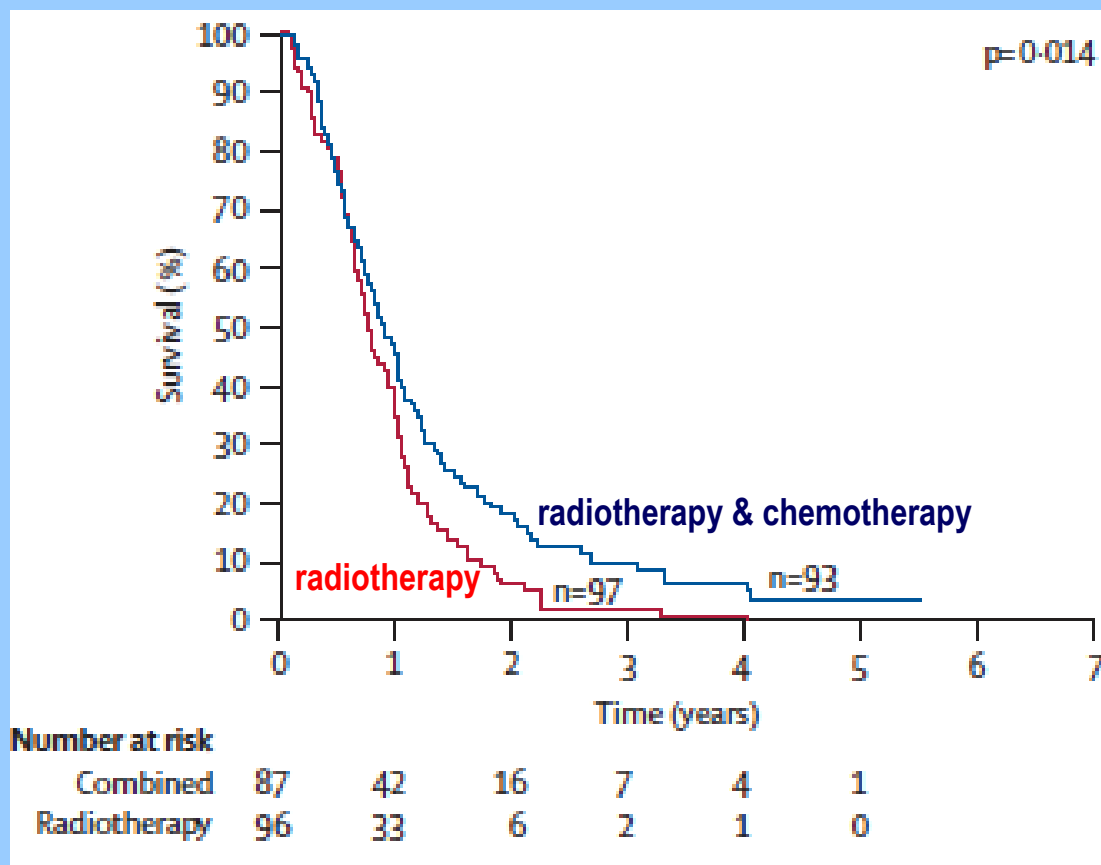
Palliative radiotherapy

Palliative radiotherapy
&

chemotherapy

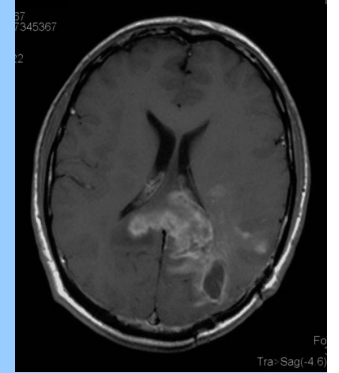
Gliomas in the elderly

Survival in RPA class V patients (age<70)



EORTC 26981/NCIC trial

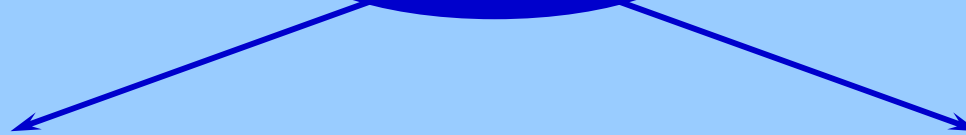
intensifying treatment



Primary glioblastoma



randomize



Chemotherapy

Chemotherapy
&

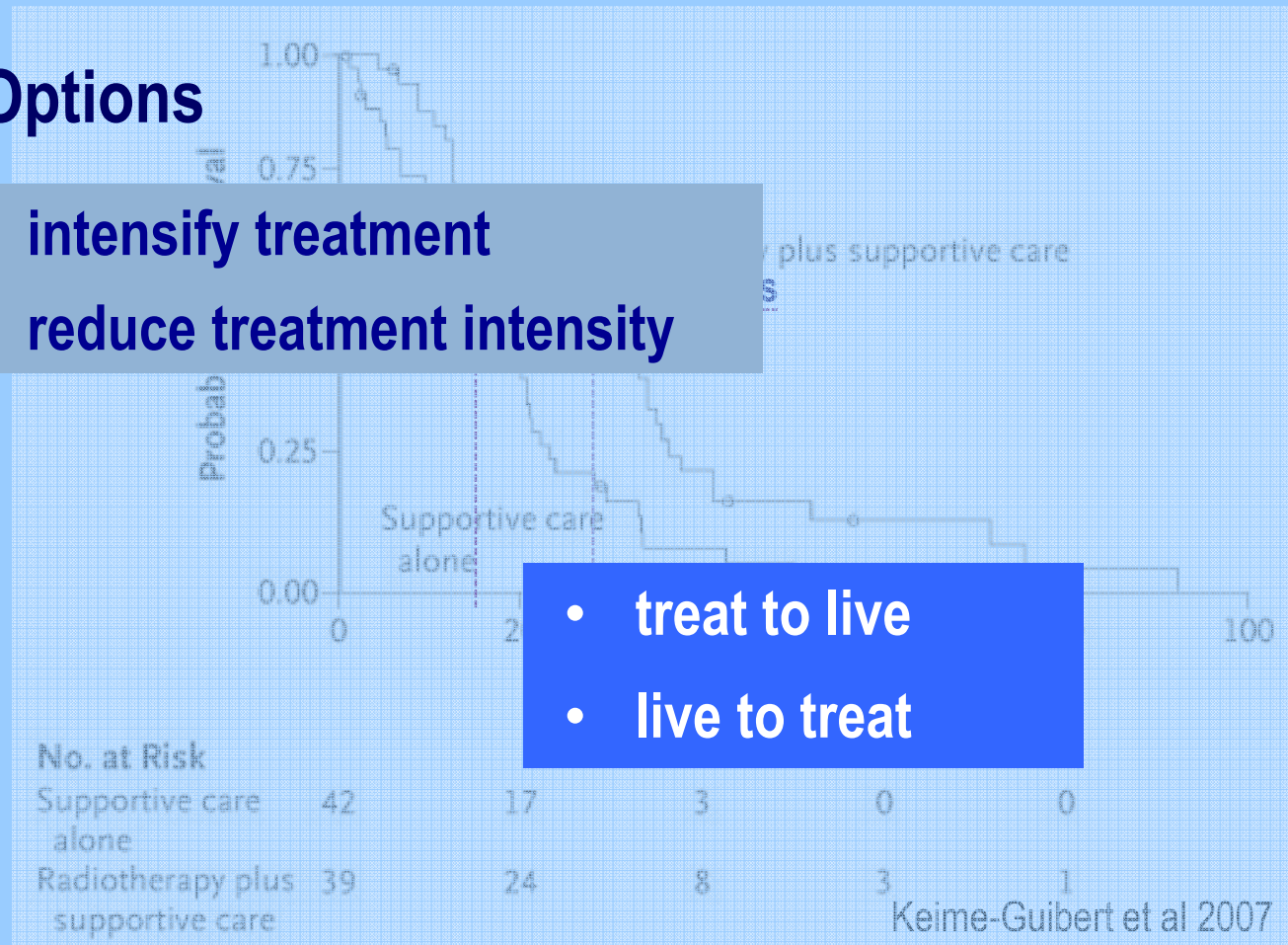
Palliative radiotherapy

Gliomas in the elderly

Where next?

Options

- intensify treatment
- reduce treatment intensity

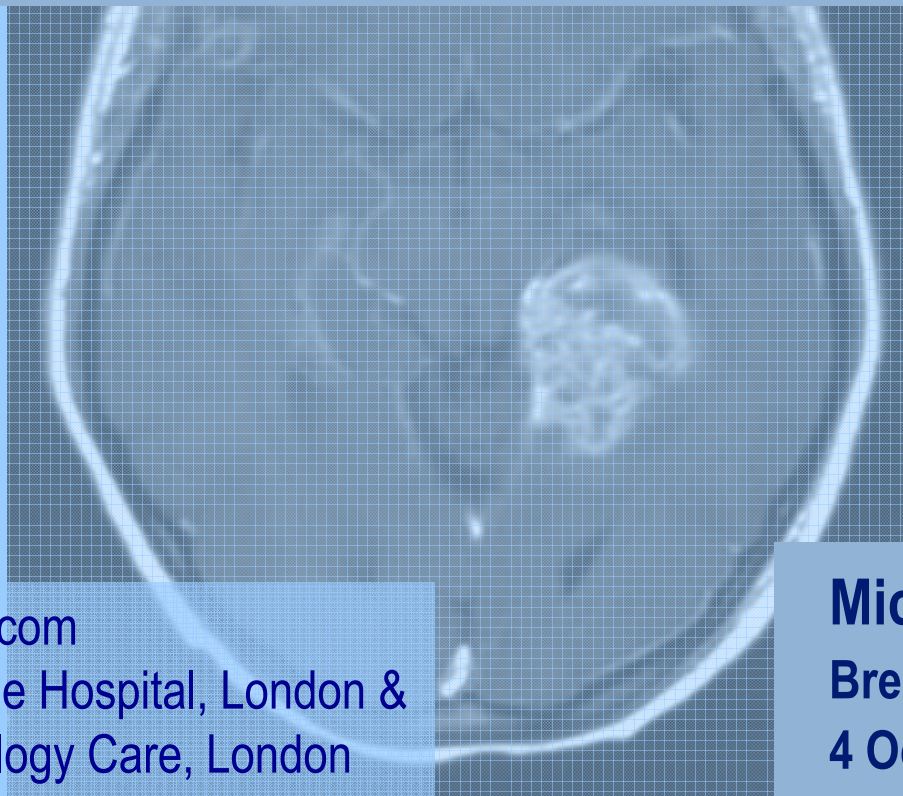


Gliomas in the elderly

From dreams to reality

Therapy of gliomas in the elderly

for palliation, after partial surgery



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Leaders in Oncology Care, London

Michael Brada

Brescia

4 October 2013